UNIVERSITY
OF MICHIGAN
MAR 28 1951
MEDICAL
LIBRARY

Volume XII MARCH 1951 No. 3

DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

CONTENTS:

INTRAVENOUS PERVITIN AND THE PSYCHOPATHOLOGY OF SCHIZOPHRENIA 67
Justin M. Hope, M.D., Enoch Callaway, M.D., and Sidney L. Sands, M.D.

SEIZURE PATTERNS IN PSYCHOMOTOR EPILEPSY 73
Leon M. Golub, M.D., Henry V. Guhleman, M.D., Jerome K. Merlis, M.D.

WITHDRAWAL EFFECTS OF SODIUM AMYTAL 77
E. J. Alexander, M.D.

DRAMAMINE IN THE PREVENTION AND TREATMENT OF NAUSEA AND VOMITING FOLLOWING ELECTROSHOCK THERAPY 83
Edward F. Kerman, M.D.

PAGET'S DISEASE COMPLICATED BY RECURRENT EXTRADURAL HEMATOMA 86
William G. Peacher, M.D.

CHILD ADMISSIONS TO A RECEIVING HOSPITAL 90
Jack V. Wallinga, M.D., and Arthur J. Bachrach, B.S.

SANITARIA

ASSOCIATE EDITORS

A. E. Bennett, M.D. ..... Berkeley, California
Francis J. Braceland, M.D. ..... Rochester, Minn.
Franklin G. Ebaugh, M.D. ..... Denver, Colorado
Temple Fay, M.D. ..... Philadelphia, Pennsylvania
Milton H. Erickson, M.D. ..... Phoenix, Arizona
Hamilton Ford, M.D. ..... Galveston, Texas
Walter Freeman, M.D. ..... Washington, D.C.
George T. Harding, M.D. ..... Columbus, Ohio
A. Hauser, M.D. ..... Houston, Texas
Louis J. Karnosh, M.D. ..... Cleveland, Ohio
Frank H. Lutes, M.D. ..... Nashville, Tennessee
Wm. Malamud, M.D. ..... Boston, Mass.
Karl A. Menninger, M.D. ..... Topeka, Kansas
Hans H. Reese, M.D. ..... Madison, Wisconsin
S. Bernard Wortis, M.D. ..... New York, N. Y.

Titus H. Harris, M.D.
Galveston, Texas
Editor-in-Chief

YEARLY SUBSCRIPTION $4.00
SINGLE COPIES 40 Cents
FOREIGN SUBSCRIPTION $4.50

George Biegeir, B.S., LL.B.
Chicago, Illinois
Managing Editor

Founded 1879

RING SANATORIUM

Eight Miles from Boston at an Elevation of 400 feet

For the study, care and treatment of emotional, mental, personality, and habit disorders.

All recognized psychiatric therapies are used as indicated.

Cottage accommodations meet varied individual needs. Limited facilities for the continued care of progressive disorders requiring medical, psychiatric, or neurological supervision.

Consultants in all Specialties

CHARLES E. WHITE, M. D.
LOUIS BRENNER, M. D.
FRED E. LAWRENCE, M. D.
Associates

BENJAMIN SIMON, M. D.
Director

ARLINGTON HEIGHTS, MASSACHUSETTS
Telephone AR 5-0081

FRANCIS W. RUSSELL
Executive Secretary

HARDING SANITARIUM

WORTHINGTON, OHIO

For Nervous and Mental Disorders

NINE MILES NORTH OF STATE HOUSE — COLUMBUS

HARRISON S. EVANS, M.D., Medical Director
GEORGE T. HARDING, M.D., President of Board
CHARLES L. ANDERSON, M.D., Clinical Director

L. HAROLD CAVINESS, M.D.
J. RUSSELL FRANTZ, M.D.
THEODORE J. LUKENS, M.D.
LESLIE H. GOULD, M.D.
CHARLES W. HARDING, M.D.

Telephone: Columbus FR. 1-8367

Compton Sanitarium

AND

Las Campanas Hospital

COMPTON, CALIFORNIA
(Near Los Angeles)

Compton Sanitarium is a private psychiatric hospital with 120 beds. Emphasis is given psychotherapy by a staff of resident psychiatrists. Other treatment procedures are duly evaluated and administered. Careful records are maintained. There are psychiatrically trained graduate nurses; student nurses through affiliation; nursing attendants; dietitian; occupational therapist; recreational therapist; hydrotherapist; masseuse. Las Campanas Hospital (43 beds) provides adjunct general hospital facilities. Compton Sanitarium and Las Campanas Hospital are approved by the American College of Surgeons.

G. CRESWELL BURNS, M.D., *Medical Director.*

BEVERLY HILLS CLINIC and SANITARIUM

For the Study and Treatment of Nervous and Mental Diseases

218 NO. WESTMORELAND — DALLAS 11, TEXAS

This sanitarium is a psychopathic hospital with a home-like environment and is equipped to treat psychiatric and neurological cases in a most scientific manner by means of psychotherapy, occupational therapy, recreational therapy, and physiotherapy, including insulin and electroshock treatments as well as neurosurgery. There is a trained psychologist as well as a trained social worker. An electroencephalographic instrument is available.

ARTHUR J. SCHWENKENBERG, M.D.
Medical Director

JOSEPH L. KNAPP, M.D.
Associate Psychiatrist and Clinical Director

JOHN C. POWELL, JR., M.D.
Associate Psychiatrist

ARCHIE R. FOLEY, M.D.
Senior Resident Psychiatrist

STEPHEN WEISZ, M.D.
ROBERT B. WINN, M.D.
Visiting Neuropsychiatrists

VOL. XII MARCH 1951 No. 3

Published monthly by
PHYSICIANS POSTGRADUATE PRESS
277 Broadway, New York 7, New York

EDITORIAL OFFICES
UNIVERSITY OF TEXAS SCHOOL OF MEDICINE
800 Avenue B., Galveston, Texas

Entered as second-class matter at the Post Office at New York, N. Y.

DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Intravenous Pervitin and the Psychopathology of Schizophrenia

JUSTIN M. HOPE, M.D., ENOCH CALLAWAY, M.D.,
and SIDNEY L. SANDS, M. D.
Worcester, Mass.

The effects of drugs on psychopathology are of both practical and heuristic concern to the psychiatrist. Practically, the evaluation and treatment of some psychiatric cases is aided by drugs. Of no less concern to the student of psychopathology is the opportunity afforded by drugs to modify certain aspects of abnormal behavior at will. With some variables under the control of the experimenter, relationships between various manifestations of psychopathology can be viewed in a new light.

The d-isomer of desoxyephedrine, known variously as Pervitin, D.O.E., Desoxyn, and Methedrine, has received considerable study. Reviews by Ivy and Boetzel,[1] and Haley[2] cover the literature in general up to 1947. More recent work on its psychiatric applications has been done by Levine, et al.,[3,4] Rudolph,[5] and Delay.[6] The papers by Levine, et al. described changes in schizophrenic psychopathology with 20 mgm intravenous injections of Pervitin. This work stimulated us to investigate the effects of the drug on the schizophrenic process in more detail, as such an investigation seemed worthwhile.

Method

The subjects selected for this study were all hospitalized schizophrenics ranging in age from 18 to 54 years, with a median of 33 years. The time between first hospitalization and study ranged from one month to 33 years, with a median of 2 years.

We first selected a group of 30 subjects, which was composed of 3 equal subgroups. Five males and 5 females were included in each subgroup. For one of these subgroups, subjects were selected because of their predominantly catatonic symptomatology; for another, subjects with overt paranoid colorings were chosen; while for the third subgroup, subjects were selected without regard for accessory symptomatology.

Each subject was interviewed in a quiet room. Evaluation of mental status was done, and the subject was rated on the psychiatric rating scale of Malamud and Sands.[7] Then 20 mgm of Pervitin in 1 cc of an aqueous isotonic solution was rapidly injected intravenously. Questions on the anticipated effects of the injection were turned back to the subject and suggestion was avoided as much as possible. After the injection, the subject was observed for from twenty minutes up to several hours, during which period mental status examinations, psychiatric evaluation, and rating scales were repeated.

The rating scale as devised by Malamud and Sands encompasses 22 functions. However, as the effect of intravenous Pervitin is quite immediate and lasts only 30 to 45 min-

From The Research Service of Worcester State Hospital and Worcester Foundation for Experimental Biology.

utes in some cases, 6 functions were deleted as they did not lend themselves to immediate cross sectional evaluation. This left 16 functions to use in rating acute changes. Figure I shows this modified rating scale. Patients can be rated from one to six on each side of a two point base line. In this study each function is considered as a fourteen point scale, and the score for change after Pervitin is taken as the difference between pre-Pervitin and post-Pervitin ratings. For evaluating changes in individual categories a shift to the left is labeled minus, while a shift to the right is called plus. The descriptive terms in Figure I define each function to some extent. However, it should be noted that we have viewed each function as a continuum between two extremes rather than relying on a given position of a particular descriptive adjective. Illustratively, let us consider a subject lying in a catatonic stupor prior to injection of Pervitin. If he were completely immobile, we should rate him at 14 under motor activity. This would be 7.5 degrees from the mid-point of the base line. After Pervitin, let us assume that he tosses about, gesticulates, and speaks, yet does not become as violently overactive as possible. We should then rate him at 4. Thus the change in "Motor Activity" would be —10. It will be noted that the series of adjectives comprising each function are not necessarily continuous nor are they mutually exclusive. However, in using this scale, the most predominant behavior is selected for scoring, with emphasis on the most deviant patterns observed.

Having observed the effects of a single injection of the drug, we then studied the repeatability of its effects. Toward this end three new patients were selected and each received serial injections with clinical observations and mental status examinations. Three additional patients were selected from our first group of thirty. They were given repeated injections three times a week for two weeks, thus receiving six additional injections. They were injected and examined by a different worker every third test. Ratings, as well as mental status examinations were done at each injection as on the single injection tests.

Results

I. General Considerations.

Responsiveness to injected Pervitin is not apparently influenced by the age of the schizophrenic subject. Figure II, however, shows that the greatest response to the drug occurs in the most recently hospitalized group. (The total score is the sum of changes in all functions regardless of direction. A score of 24 was arbitrarily taken to delineate clearly responsive subjects from those in whom the response was equivocal. This figure is also equivalent to a 4-point

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
FUNCTION	6	5	4	3	2	1	BASE LINE		1	2	3	4	5	6
MOTOR ACTIVITY	Excited		Agitated		Restless		ACTIVE	QUIET	Under-Active		Retarded			Stuporous
MIMETIC EXPRESSION	Incongruous		Dramatizing		Exaggerated		ANIMATED	RESTRAINED	Stiff		Waxy-Flexibility			Mask-Like
RESPONSIVITY	Anaklitic		Suggestible		Dependent		FLEXIBLE	RIGID	Stubborn		Resistive			Negativistic
HOSTILITY REACTIONS	Destructive		Combative		Belligerent		AGGRESSIVE	SELF-EVADING	Self-Deprecating		Self-Mutilating			Suicidal
ATTENTION	Uncontrolled		Markedly Distractible		Moderately Distractible		ALERT	DETACHED	Preoccupied		Disparative			Completely Withdrawn
AWARENESS	Confused	Scattered (Disoriented)	Splitting		Superficial		DIFFUSE	RESTRICTED	Perplexed	Depersonalization	Cloudy (Disoriented)			Unconscious
SPEECH	Incessantly Productive		Push-of-Speech		Over-Talkative		VOLUBLE	TERSE	Under-Talkative	Retarded	Blocking			Mute
ASSOCIATIONS	Echolalia		Klang		Abrupt		DIRECT	INDIRECT	Vague-Circumstantial	Tangential	Irrelevancies			Neologisms
MOOD	Exhilarated		Euphoric		Enthusiastic		OPTIMISTIC	PESSIMISTIC	Somber		Despondent			Deeply Depressed
AFFECT	Inappropriate		Explosive		Labile			RESERVE	Inadequate		Bland			Flat (Rigid)
FEELING	Panic	Anxious	Tense		Hypersensitive		SENSITIVE	CASUAL	Phlegmatic		Dull			Apathetic
PERCEPTION	Hallucinations		Illusions Pseudo-Hallucinations		Exaggerated Intensity		EXTERO-CEPTIVE	INTERO-CEPTIVE	Self-Observation	Hypochondriasis	Conversions			Somatic Hallucinations
THOUGHT PROCESSES	Fragmented		Alogical Paralogical		Illogical		SHALLOW	CRITICAL	Rationalizing		Obsessive Hair-Splitting			Obsessive Doubt
SUBJECTIVE REORGANIZATION	Cosmic Del. (Omnipotence)	Del. of Grand.	Ideas of Per.	Ideas of Influ.	Ideas of Ref.	Autistic	EXTRA-PERSON REFERENCE	INTRO-PERSON REFERENCE	Ideas of Inferiority	Self-Accusatory	Somatic Delusions			Nihilistic
MEMORY	Confabulation		Fabrication		Obsessive Reminiscences		PRECISE SCRUPULOUS	CARELESS VAGUE	Over-Generalizing		Gaps			Deteriorated
INSIGHT	Negation of Problem	Problem Exogen.	Recog. of Prob. Without Concern		Shifting of Blame		SELF-SATISFIED	SELF-CRITICAL	Self-Hyper-critical	Add. of Non-Exist. Probs.	Despairing Self Blame		Attitude of Guilt Helplessness	

Fig. 1. The psychiatric rating scale of Malamud and Sands as modified for use in this study.

change in each of the 6 functions significantly modified by Pervitin, as will be described later.)

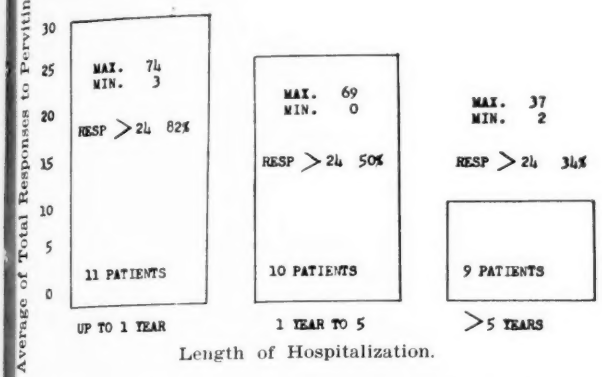


Fig. 2. The average of the total response to injected Pervitin in schizophrenic subjects of varying lengths of hospitalization.

II. Rating Scale Evaluation of Functions as Modified by Pervitin.

Changes of each function in our group of 30 patients are dealt with separately in Table I. In this table, changes in each direction are totaled separately under "change." The algebraic sum of "change" is divided by thirty to give the average change. It will be noted that motor activity, mimetic expression, and speech show significant changes. Reference to Figure I indicates that these sponsivity, affect, and feeling. Reference to Figure I indicates that this represents a change from resistive, bland, and phlegmatic behavior in the direction of more flexible demonstrative and sensitive behavior. Thus, subjects demonstrating this change became less emotionally withdrawn after Pervitin. These six functions show an average change changes bespeak increased activity in general. Significant changes also occur in re- of two points or more. The other functions change less markedly and less regularly. In the function labeled hostility the trend is toward more belligerent behavior. Attention shows some change as withdrawn patients become more accessible. In awareness the trend is in the direction of less restriction. The changes in associations are in the direction of greater vagueness and tangentiality. In the following categories: perception, thought processes, and subjective reorganization, in general, our subjects exhibited more pathology after the injection of Pervitin. Mood shows an inconstant change which is in the direction of a more optimistic outlook. The change noted in memory is in the direction of greater preciseness. Insight shows a change as some patients admitted the existence of problems only after Pervitin.

Catatonic patients did not differ strikingly from paranoid patients in their over-all response to the drug. However, they did show differences in degree of change in certain functions. Taking "change" for catatonics and paranoids separately as we did for the group in Table I, we find catatonics responding more in motor activity (—17 as opposed to —13 plus 2 for paranoids), and mimetic expression (—28 plus 1 as opposed to —15 plus 4). Paranoids on the other hand responded more in affect (—35 as opposed to —16 for catatonics) and feeling (—22 as opposed to —6). Thus catatonics tended to show less of the usual immobility, both in mimetic expression and general motor activity, whereas paranoids became less bland, with increasing tenseness in some cases.

III. Mental Status Illustrations of Rated Changes.

In many of our observations affective changes have been most striking. Bland paranoid subjects who previously described

TABLE 1

	Change	*Average Change*		*Change*	*Average Change*
Motor Activity	—62 + 2	—2.0	Mood	—18 + 11	—0.3
Mimetic Expression	—67 + 5	—2.0	Affect	—95	—3.1
Responsibility	—71 + 3	—2.3	Feeling	—65 + 4	—2.0
Hostility	—14 + 3	—0.4	Perception	—16 + 12	—0.1
Attention	—25 + 9	—0.5	Thought Processes	—27 + 5	—0.7
Awareness	—14 + 5	—0.3	Subjective Reorg.	—12 + 6	—0.2
Speech	—80 + 7	—2.4	Memory	—11	—0.3
Associations	—15 + 19	0.1	Insight	— 5 + 28	0.8

TABLE I. Change observed after Pervitin, tabulated for each function separately. See *Results* for explanation.

their delusional tortures without affect, frequently wept and became very emotional after the injection. One mute catatonic cried and pleaded with his examiner to give him affection. He spoke with emotion of his extreme loneliness and feelings of isolation. Actual historical data as well as thought content became more accessible after Pervitin. Some of our subjects were quite guarded, and delusions which were suspected from previous interviews could not be elicited at all. On injection of Pervitin such patients became more communicative and exhibited greater affective response. Also in such cases the subject expressed more delusional material and peculiar associations while thinking was disorganized. It is difficult to attribute this finding to a specific cause. There are at least three possibilities. First, such subjects may have been thinking in such a way before Pervitin and not expressing their thoughts; secondly, the increased affective reaction and push of speech might in itself have produced some disorganization of thought; and thirdly, Pervitin itself may exert a selective effect on these functions. Occasionally, however, subjects who expressed more delusional material were then able to question the validity of a few of their ideas while under the influence of this drug.

It should be mentioned that two subjects showed no observable change at all on injection of Pervitin, and one catatonic showed some increased cerea flexibilitas. Two subjects were tearful, withdrawn and agitated for several days after the injection of Pervitin. One subject stated that he was upset by the things he said under Pervitin. No subject showed what could be called clinical improvement after the immediate affects of the injection passed.

IV. Results of Repeated Injections.

As an exploratory study, two paranoid female subjects were given repeated injections. One subject received four injections at weekly intervals, while the other received eight injections, one every other day. Each subject continued to respond to the drug. No ill effects were noted other than occasional sleeplessness and agitation following these injections. A third subject, a catatonic male, responded very strikingly to Pervitin on the first injection. He became hyperactive, tearful, and expressed bizarre ideas. He voluntarily took food for the first time in several days. He reached out for contact with his doctors. Several hours later he lapsed back into catatonia. An injection of Pervitin was repeated two days later and produced minimal effect, two subsequent injections at two day intervals produced no change whatsoever.

Three additional patients were selected from our first study group. Two had shown an active response to Pervitin, while one had shown a borderline response. The serial injections were performed as was the initial injection study. Our findings are illustrated in Figure III. Sex, age, and date of admission to the hospital are given for each patient. The boxes indicate the total score of the change after injection. The circles are included as an indication of the general status of the patient before injection. They represent the sum of the number of points from the center of the base line to the preinjection rating. The initials H and

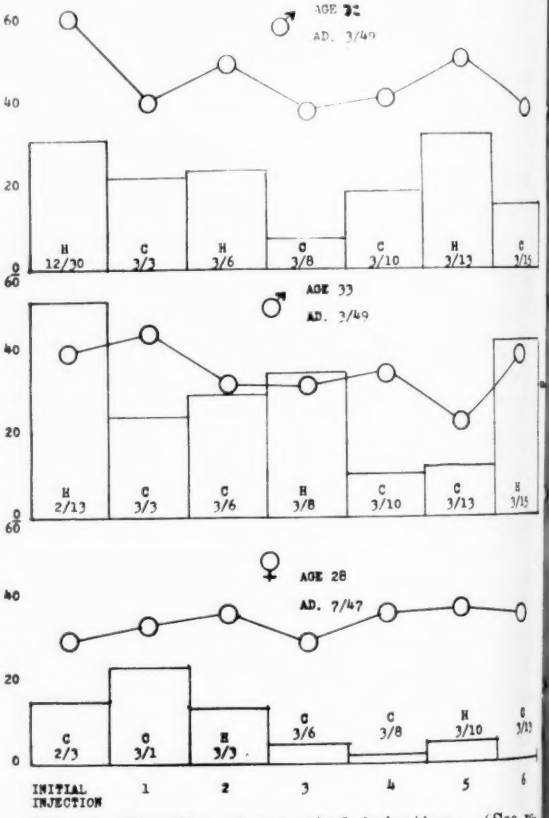


Fig. 3. Results of repeated injection. (See results for explanation.)

C indicate the worker who performed each rating.

The two responsive individuals remained relatively responsive to repeated injections, while the poorly responsive individual eventually showed no response.

Discussion

From our study of Pervitin certain observations are pertinent. Schizophrenic subjects become more communicative after its injection. Delusional material and pathological thought processes become either accentuated or more accessible. Affective responses become more appropriate. Equally important, although more difficult to describe, is the increase in what we called "contact with the examiner." Many of our subjects were more willing to explain their beliefs and feelings after Pervitin. They gave previously withheld historical material and some expressed a desire for help. In general, there was a "reaching out" on the part of the patient for contact with the examiner.

These findings suggest that this drug may be used to somewhat the same purpose as sodium amytal, for both drugs will occasionally enable an examiner to obtain more information from a patient in a given length of time. However, there are many differences. Practically, the rapid injection of a given dosage of Pervitin is more convenient than a slow injection of a variable dosage of sodium amytal. With amytal the patient may go to sleep before the interview is well begun or may have an amnesia for the material discussed. Pervitin, on the other hand, may produce enough sleeplessness to necessitate a sedative at bedtime, and the painful memory of the Pervitin interview may be quite upsetting to some patients.

Gottleib, et al.[8] report that about fifty per cent of schizophrenic subjects show diminished psychopathology on the first injection of amytal. But tolerance develops rapidly and becomes complete by the seventh day of repeated injections. We find a roughly comparable initial response (17 out of 30 responded greater than 24 points on the rating scale) but there is no similar rapid development of tolerance in most initially responsive individuals. Statistically we would expect more patients in our group hospitalized up to one year to recover from their illness than in the group hospitalized for over five years. And it is in the acute group, with its better prognosis, that we find the greatest response to Pervitin. This is interesting in view of the work of Gottleib and Hope[9] on the prognostic value of amytal.

This drug definitely facilitates the psychiatric examination of uncommunicative schizophrenic subjects as it does make them more accessible to the interviewer. However, we can make no statement as to the therapeutic usefulness of this drug.

Our findings in general are in agreement with the observations of others who have worked with this drug on schizophrenics. Delay[6] using 30 mgm intravenous injections of Pervitin for what he calls "Methedrine Shock" reports that schizophrenic psychopathology is accentuated by the drug particularly in relationship to the Rorschach responses. Whereas amytal increases the performance ability of schizophrenics (Layman[10]), Delay reports that Pervitin has the opposite effect. He speaks of amytal as a *"psycholeptic,"* and of Pervitin as a "psychogogue." However, he noted a general increase in cerea flexibilitas when catatonics were given his "Methedrine Shock." We observed this in only one case. Fleugel,[11] using dosages of 3 to 4 mgm by mouth, noted that 5 out of 10 stuperous schizophrenics responded by walking, talking, and eating for a few hours. He also noted that the effects were not always repeatable. These findings seem to correspond to our observations in spite of differing dosage and administration. Levine, et al.[3,4] have also noted that psychiatric patients given 20 mgm of Pervitin intravenously become more responsive and communicative.

Regardless of the value or lack of value of Pervitin in the management of patients suffering from schizophrenia, in this work as well as the work of other investigators a significant observation is apparent, i.e. a chemical agent can exert an influence on the schizophrenic "process." The value of this observation can be explored only by further study. It appears worthwhile to study the effects of chemical agents, of known pharmacodynamics, on subjects suffering from

recognizable psychiatric diseases. Studies of this type may prove fruitful in that they may shed some light on the nature of the disease "process" itself. An understanding of the disease process is of particular importance in those psychiatric diseases which in the present state of our knowledge are grouped under the "functional" mental disorders.

Summary

A. Using the psychiatric rating scale of Malamud and Sands as an aid to clinical study, observations on the intravenous administration of 20 mgm of Pervitin to schizophrenic subjects revealed changes in certain aspects of objective behavior.

1. An increase in *motor activity* was observed. This is most striking in catatonic patients showing motor retardation, although it is observed in others as well.

2. *Mimetic expression* became more animated in stiff bland patients.

3. Lessening negativism and resistiveness was observed, with increasing *responsiveness* to the examiner.

4. *Speech* was increased to the point that some patients showed a real "push of speech."

5. *Affect* became more appropriate, particularly in bland paranoid subjects, who even showed some lability of affect after injection.

6. Phlegmatic subjects showed more signs of tension.

B. We have noted variability in the response of the same patient to this drug, but no clear tolerance seems to develop.

C. We have not infrequently observed an increase in thinking disturbances while affect has become more appropriate.

Pervitin Hydrochloride was supplied through the courtery of Smith, Kline, and French Laboratories.

BIBLIOGRAPHY

1. Ivy, A. C., and Goetzl, F. R.: d-Desoxyephedrine: A Review. *War Med.*, 3: 60-77, Jan., 1943.
2. Haley, T. J.: Desoxyephedrine: A Review of the Literature. *J. Am. Pharm. A.* (Scient. Ed.) 36: 161-169, June, 1947.
3. Levine, J., Rinkel, M., and Greenblatt, M.: Physiological and Psychological Effects of Intravenous Pervitin. *Am. J. Psychiat.*, 105: 429-434, December, 1948.
4. Levine, J., Rinkel, M., and Greenblatt, M.: Pervitin in Neuropsychiatry: Comparison with Sodium Amytal and Amphetamine Sulphate. *Arch. Neurol. and Psychiat.*, 63: 351-352, February, 1950.
5. Rudolf, G. deM.: The Treatment of Depression with Desoxyephedrine (Methedrine). *J. Ment. Sc.*, 95: 920-929, October, 1949.
6. Delay, Jean: Pharmacological Explorations of the Personality; Narco-analysis and Methedrine Shock. *Proc. Roy. Soc. Med.*, 42: 491-496, July, 1949.
7. Malamud, W., and Sands, S. L.: A Revision of the Psychiatric Rating Scale. *Am. J. Psychiat.*, 104: 231-237, October, 1947.
8. Gottlieb, J. S., Krouse, H., and Freidinger, A. W.: Psychopharmacologic Study of Schizophrenia and Depressions, II. Comparison of Tolerance to Amytal and Amphetamine Sulphate. *Arch. Neurol. and Psychiat.*, 54: 372-377, Nov.-Dec., 1945.
9. Gottlieb, J. S., and Hope, J. M.: Prognostic Value of Intravenous Administration of Sodium Amytal in Cases of Schizophrenia. *Arch. Neurol. and Psychiat.*, 46: 86-100, July, 1941.
10. Layman, J. W.: A Quantitative Study of Certain Changes in Schizophrenic Patients Under the Influence of Sodium Amytal. *J. Gen. Psychol.*, 22: 67-86, January, 1940.
11. Flügel, F. E.: Medikamentöse Beeinflussung Psychischer Hemmungszustände. *Klin. Wchnschr.* 17: 1286-88, 1938.

Seizure Patterns In Psychomotor Epilepsy

LEON M. GOLUB, M.D., HENRY V. GUHLEMAN, M.D., JEROME K. MERLIS, M.D.
Framingham, Massachusetts

A multitude of phenomena has been classified as psychomotor epilepsy. According to Gibbs,[1] "Psychomotor epilepsy is a specific epileptic syndrome characterized by clinical psychomotor seizures and by an epileptic type of involvement of the anterior portion of the temporal lobe, as evidenced by a focus of spike seizure activity in that area. . . ." However, the clinical manifestations of what is to be called psychomotor epilepsy are not clearly defined. Frequently it is difficult to decide, on clinical grounds, whether a given episode of bizarre behavior is a manifestation of epilepsy or of some specific psychiatric disorder such as a fugue state or hysterical seizure. It was, therefore, considered that a detailed study of the clinical seizure phenomena appearing in a group of patients diagnosed as having psychomotor epilepsy might contribute information of value.

No data are available concerning the incidence of anterior temporal spike foci in patients clinically diagnosed as psychomotor epilepsy, but Gibbs[2] has reported that of 163 patients with epilepsy whose EEGs showed anterior temporal spikes, 95% had a history of seizures which were classified as psychomotor epilepsy. We have accordingly selected for study a group of patients on the basis of two criteria: (1) that they manifest paroxysmal episodes of non-convulsive disturbance of behavior with amnesia for all or part of the attack; and (2) that they show anterior temporal spikes or sharp-wave activity in the interseizure electroencephalogram, awake or asleep. Although this selection may include only a special group of what has been called psychomotor epilepsy by others, it was felt that it would probably exclude patients with episodic bizarre behavior of psychological origin.

The group consists of 21 patients, two who have psychomotor attacks alone and 19 who have psychomotor attacks with other types of seizures, as shown in Table I.

TABLE I

TWENTY-ONE PATIENTS WITH ANTERIOR TEMPORAL SPIKES

Type of Seizure	*No. of Patients*
Psychomotor alone	2
Psychomotor predominantly, Grand Mal occasionally	8
Psychomotor occasionally, Grand Mal predominantly	4
Psychomotor and Grand Mal, equally	6
Psychomotor and Focal Motor, equally	1

In four of the patients there was evidence of structural brain pathology. Three other patients had psychotic manifestations and six manifested rather definite personality disorders. In addition there was one patient with a history of sleep paralysis and another who had a congenital reading disability.

Seizure descriptions of the psychomotor attacks of the 21 patients were obtained from several sources. The most reliable descriptions came from observations made during the patients' stay in the hospital. Descriptions were also obtained from the patient's relatives or others who had witnessed attacks. In almost all cases detailed descriptions of several seizures were available.

Consideration of this detailed information indicated that the psychomotor attacks showed a more or less specific sequence of events. The phenomena at the very beginning were very brief, appeared and disappeared abruptly, and commonly consisted of what might be termed a suspension of activity. Typically, the patient would stare and there might be a single movement which took such forms as extension of a limb, turning of the head to one side, or changing from a reclining to a sitting position. No repetitive activity was present at this stage. Following the initial phenomena, the patient might show lip smacking, licking, or rubbing; he might pick at his clothing or grope; or there might be erratic repetitive movements of his arms or legs. It was only later that more integrated, almost purposeful, be-

From the National Veterans Epilepsy Center and the Neurological Service, Cushing Veterans Administration Hospital, Framingham, Mass.

havior was manifested. This might consist of apparently purposeful searching, confused speech, walking, wandering or other more complicated activity.

The following are several examples of some of the seizures which were observed and which illustrate the points just mentioned:

J.B., while in the physician's office, suddenly stopped talking, looked off into space, staring. He slumped down in his chair for a brief moment, then sat up and began to rub his abdomen with both hands. A flashlight was shined into his eyes and he turned away. He began to rummage about the desk as if looking for something. When questioned as to what he wanted, he said, "I wanna, I wanna." At this point he took a cigarette from his pocket, lit it, and started to smoke. He then got up from his chair, walked out of the office, wandered down the hall opening all the doors saying, "I want a toilet." Next he walked down the hall, but could not be distracted by any outside contact. He then lay down on the bed and appeared to regain contact gradually.

R.C. was noted to have seizures while on the ward characterized by cessation of conversation and staring straight ahead, followed by chewing, blinking, grimacing, and copious drooling. These were followed by groping movements of the hands and then gradual return of awareness. A typical episode of this same patient's seizures was described as follows: His eyes were glazed and staring straight ahead for several seconds, then there was considerable drooling and chewing movements of the jaws, followed by groping movements of the hands with the rest of the body relaxed and limp. This progressed to blinking and grimacing. Toward the end of the seizure the patient laughed without apparent cause for a minute or two. The whole episode lasted four or five minutes.

Patient C. W. frequently had an aura consisting of a flushed feeling and a tingling sensation in the upper half of his body. There might be a feeling of warmth beginning in his abdomen and ascending. When the tingling and warmth reached his neck and head, he would lose awareness. In most of the attacks, the patient would stare, and then turn his head to one side or the other. After the head turning had begun, he would rub himself or nearby objects repetitively with his right hand. Most frequently he would repeatedly rub his abdomen or genital area, and the rubbing would be accompanied by smacking of his lips. After the lip-smacking and rubbing had begun, he might wander through the corridor. During this period another patient might lead him back to his bed.

P.P.: The patient was noted to be sitting motionless in bed looking bewildered for about 15-20 seconds. There was then smacking of the lips and after a short time the patient got off his bed and looked at a couple of other patients, meanwhile talking and muttering incoherently. He began to clap his hands just before the episode was over. In other episodes the lip-smacking and confused muttering have been followed by efforts to open doors, getting into the wrong bed, and searching through drawers and under the bed.

M.Y.: The patient was playing golf with another patient when he suddenly jerked his head to the left, did not cry out or fall, but stared dazedly. After a while, he began to call the other patient "Daddy," and attempted to strike him. At another time the patient was noted to be staring momentarily and then began to kick a basket repeatedly with his left foot. Finally he got up and wandered around muttering unintelligibly for several minutes. At another time, while playing cards, the patient suddenly stopped, stared into space, slumped in his chair and then appeared confused for a period of about five minutes.

O.S.: The patient was found sitting up in bed staring into space and was not responsive. The nurse then noted erratic movements of his arms and right leg. He grabbed his thighs, and arched backwards, swaying back and forth. He began to hum and whistle and removed the bed coverings from his bed, searched through every inch of the blanket and continued to hum and whistle. He was not responsive for several minutes longer.

TABLE II

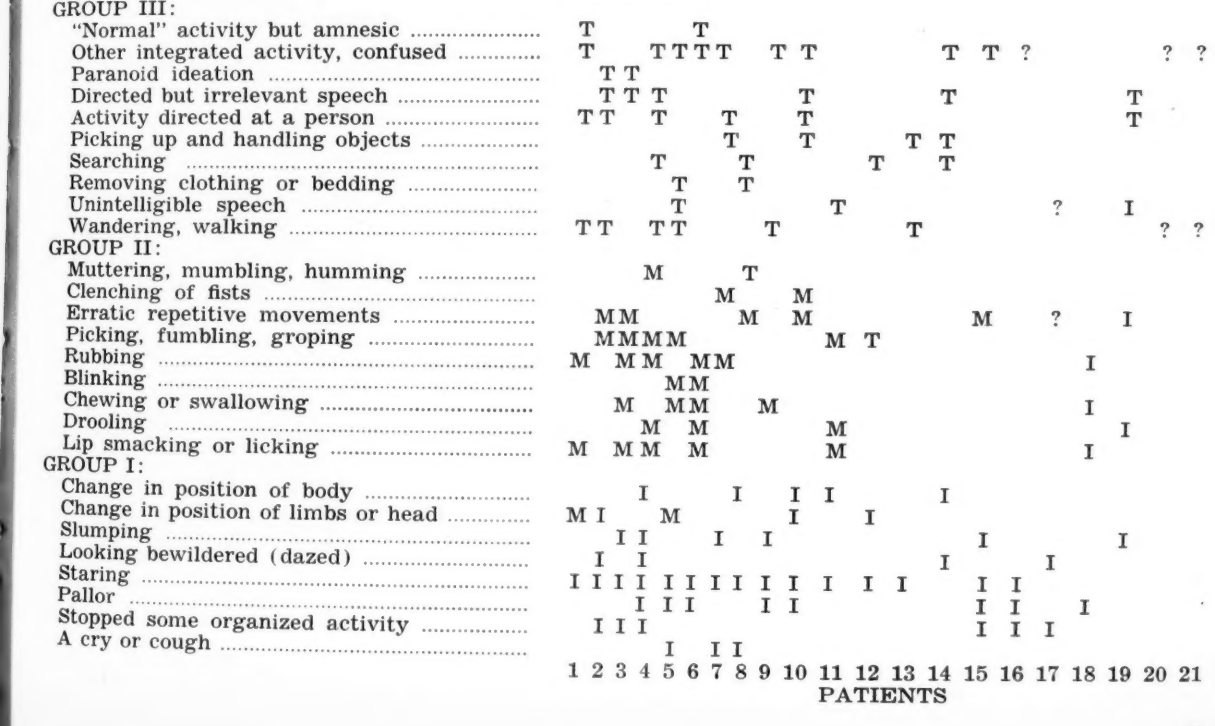
	No. Pts. showing each activity
GROUP III:	
"Normal" activity but amnesic	2
Other integrated activity, somewhat confused	12
Paranoid ideation	2
Directed but irrelevant speech	6
Activity directed at a person	6
Picking up and handling objects	4
Searching	4
Removing clothing or bedding	2
Unintelligible speech	4
Wandering, walking	8
GROUP II:	
Muttering, mumbling, humming	2
Clenching of fists	2
Erratic repetitive movements	7
Picking, fumbling, groping	6
Rubbing	6
Blinking	2
Chewing or swallowing	5
Drooling	4
Lip smacking or licking	6
GROUP I:	
Change in position of body	5
Change in position of limbs or head	5
Slumping	6
Looking bewildered (dazed)	4
Staring	15
Pallor	8
Stopped some organized activity	6
A cry or cough	3

All the phenomena recorded in the seizure descriptions were tabulated and it was found that they appeared to fall into three groups classified according to their complexity. The three groupings are shown in Table II.

Group I includes seizure manifestations which were simple in type, consisting largely of a suspension of activity with staring and perhaps with a single movement of the trunk, head, or limb. It will be noted that none of these phenomena are of a repetitive or highly organized nature. The second group consists of repetitive, apparently primitive, motor phenomena which were rarely purposeful, such as lip smacking, chewing, rubbing, fumbling or picking movements. The third group consists of more purposeful and more highly organized, activity, such as wandering, undressing, searching, confused speech, and other more complex activity. Within each group the arrangement was somewhat arbitrary, but it was felt that when any group as a whole was compared with the other groups, there was a definite difference in complexity.

In an effort to determine whether or not there was any correlation between the time of onset of each activity in a given attack and its complexity, the chart shown in Table III was made. For each patient, each kind of behavior manifested in his attacks was plotted according to its time of onset in the seizure. The phenomena that occurred initially or very early and terminated abruptly were plotted as "I" (initial). Activities that occurred after the onset of the seizure and which blended into other seizure activity were plotted as "M" (middle). Behavior which appeared later in the seizure and continued until the episode was over was considered terminal and was plotted as "T." In Table III it will be noted that the majority of "I's" are opposite the bottom group, most of the "M's" are opposite the middle group and most of the "T's" cluster opposite the third group. Where detailed data as to chronology were not available for a given manifestation, it was plotted as "?". In several of the patients, a number of different activities were recorded as being observed at the same time and these were plotted as "I" with some reservation because it was felt that the actual onset of the attack may not have been observed. In this regard it is to be noted that whereas at times complex activity was sometimes recorded as occurring initially, none of the simple phenomena listed in the first group ever occurred in the seizure after stereotyped repetitive behavior had begun. Similarly, the onset of the repetitive, stereotyped behavior, such as lip-smacking or grimacing, almost never was seen after the more integrated and more complex behavior occurred.

TABLE III



Discussion

The data presented suggest that in psychomotor attacks three phases of activity occur in chronological sequence. The initial phase is brief, usually lasting from 5 seconds to 2 minutes, and begins and ends abruptly. The phenomena observed may perhaps best be characterized as a suspension of activity. In this phase, there may be a single gross movement of the trunk, limb, or head, but there are no repetitive movements. The behavior in the first phase may be very similar to that seen in a petit mal attack. The middle phase is characterized by repetitive, stereotyped activity which shows little variation from seizure to seizure and which bears little reference to the environment. In the third, or last phase, the behavior is more complex and requires the coordination of a sequence of movements. It appears to be at least semi-purposeful and is much more variable than the other phases. In this third phase the patient is more apt to deal with objects and people in the environment and may be responsive to verbal stimuli, often inappropriately. Amnesia for this stage may or may not be complete. Behavior in the third phase is very reminiscent of post-ictal clouded states and, like the latter, disappears by gradual blending into normal activity with little of the abruptness that characterizes the ending of the initial phase.

The possibility that only the early phenomena are actually the ictal manifestations is deserving of further investigation. Of interest in this regard are electroencephalographic observations recorded during psychomotor seizures, as reported by Denis Hill.[3] These data indicated that the actual electrical seizure discnarges usually did not last more than 80 to 100 seconds and only when the rhythmical discharges were replaced by presumably post-ictal irregular low voltage slow activity did he observe what he called automatic semi-purposive behavior. It is tempting to speculate on the possibility that the 80-100 second seizure discharge correlates with the initial period we have described as suspension of activity. Investigation of this point is in progress.

The data presented suggest that the defining of psychomotor epilepsy in terms of the conspicuous manifestations such as semi-purposeful activities or confusion states may well be questioned, since such phenomena represent only the late and variable phases of the clinical picture and, possibly, are post-ictal in nature. The less variable earliest phase, best characterized as a suspension of activity, may represent a more fundamental manifestation of the psychomotor seizure discharge.

Summary

1. A detailed study of the seizure patterns was made in a group of 21 patients who had anterior temporal spike activity in the EEG and who manifested paroxysmal episodes of non-convulsive disturbance of behavior with complete or partial amnesia.

2. In the psychomotor attacks observed, three phases of activity occur in chronological sequence. The first phase is characterized as a suspension of activity, similar to the petit mal attack. The second phase is one of repetitive, stereotyped activity which shows little variation from seizure to seizure. In the third phase, behavior is complex, semi-purposeful, and variable, involves interplay with the environment, and gradually merges into normal behavior.

3. It is suggested that psychomotor seizures should not be defined in terms of the more conspicuous manifestations of the third phase, since these may be post-ictal in nature.

REFERENCES

1. Gibbs, E. L., Gibbs, F. A., and Fuster, B.: Psychomotor epilepsy. *Arch. Neuro. & Psych.*, 1948, 60:331-339.
2. Gibbs, F. A.: Ictal and non-ictal psychiatric disorders in temporal lobe epilepsy. *J. Nerv. Ment. Dis.*, In press.
3. Hill, D.: The electroencephalographic concept of psychomotor epilepsy. A summary. IVe Congres International de Neurologie. Rapports. *Masson et Cie*, Paris, 1949, 1:27-33.

Authors' Note: This paper has been reviewed in the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Withdrawal Effects of Sodium Amytal

E. J. ALEXANDER, M.D.
Detroit, Michigan

This report is to describe what our further therapeutic use of prolonged sodium amytal narcosis, as modified by Heldt,[1] has taught us concerning the withdrawal effects. A later report will be devoted to our current evaluation of the therapeutic results. In brief, the method is as follows: Sodium amytal is given, intravenously and orally, in amounts sufficient to keep the patient asleep about 16 of the 24 hours, for 7 to 12 days. The usual total amount of amytal per day averages 60 grains, but daily doses of 100 grains or more are not uncommon. Whenever a sufficiently long narcotic period has been obtained, and it can be demonstrated that successive intravenous administrations of 15 grains of the drug have less sleep producing power than before, it is discontinued abruptly. Simultaneously, fluids are limited to approximately 1500 cc. per day.

During the next 24 hours, somnolence gradually wears off, and as it disappears one observes a number of very striking signs and symptoms. There is absolute insomnia, which lasts from 24 to 96 hours; there is marked tremor of the voluntary muscles, which becomes more apparent when voluntary movement is attempted; in the period from 36 to 60 hours after cessation of the drug in about 10% of the cases, there occurs one or more generalized convulsions; and the patient experiences vivid visual hallucinations. Sometimes the hallucinations consist of pleasant or unpleasant colors; at other times images or "visions" are seen. The patient often has an unusual sensitivity to sounds, and auditory illusions and hallucinations occur, but less frequently than visual hallucinations. The patient usually develops definite delusions during his hallucinated period. Sometimes these remain fixed during the entire delirious episode, and are so vivid that they are rejected as unreal only after several days of doubt, after the delirious phase. More frequently the delusions are not fixed, and the ideas making up the mental content shift rapidly from moment to moment. The speech is affected, from a motor standpoint, by the generalized tremor present; but in addition there is often a jumbling and repetition of words, phrases, or syllables, so that the meaning is not coherent. Of course, the verbal productions are colored by the delusions developed.

The general impression gained is that the brain is in a state of hyperactivity, in a disorganized, uncoordinated way, so that there is indiscriminate discharge over the motor system, leading to tremor and convulsion; there is disturbance in the association centers so that thought is disorganized and words tumble through the mind in disconnected fashion; there is excitation of the sensory areas, so that hyperacusis, heightened response to stimuli, and hallucinations appear; and there is general over-reactivity of the brain so that sleep is impossible.

Although there are individual variations in the behavior of the patient, in his mood, in the nature of his hallucinations, and in the content of his delusions (all of which can be explained by differences in the personality of the individual patients, as well as by differences in the psychiatric syndrome for which the treatment is being administered), the insomnia, the tremor, and the delirioid hallucinations are so constant that we interpret them to be the direct result of the withdrawal of sodium amytal after its constant presence in the body for about ten days. Whether we speak of these phenomena as indicating a "toxic" reaction to sodium amytal, as a "complication" of the treatment, as an evidence of "addiction" to sodium amytal, or as "withdrawal effects" depends primarily upon how we use those terms.

"Withdrawal effect," or "complications?" Palmer[2,3] used a similar method of sodium amytal narcosis, but discontinued the drug gradually over several days. He observed these same phenomena at the time of terminating the narcosis. However, he called

From the Division of Neuropsychiatry, Department of Medicine, Henry Ford Hospital, Detroit, Michigan.

these symptoms, including convulsions, "complications." He does not disagree, in his 1937 article, with the opinion he expressed in 1932, that the "treatment has not produced any toxic effects," and "no withdrawal symptoms have been noted." He pointed out that the particular "complications" I am considering could be "avoided by a slow reduction in the dose of sedative." There is therefore no disagreement in our facts, but merely in the terms we use. To him, these symptoms were "complications," and he wished to avoid them. To us, the term does not apply because we believe the delirious episode has therapeutic effect and we therefore deliberately set out to produce it. To us, urinary retention, or fever, or a bruise the patient receives by falling while under the influence of the sodium amytal, are all properly classed as "complications" of the treatment, but the tremor, hallucinations, and sleeplessness, which reach their peak after discontinuing the drug, which can be markedly diminished if the drug is discontinued slowly rather than abruptly, and which disappear spontaneously in about three to five days, are more properly considered to be "withdrawal effects."

"Withdrawal effect," "abstinence irritability," "addiction," and "physiological dependence." These are all essentially equivalent terms. If an animal has been given a drug regularly, and then is denied it for a day or two, certain signs and symptoms may appear. The general term I use for these is 'withdrawal effect." One of these withdrawal effects is "abstinence irritability": the animal reacts, when abstinent 24 hours, with greater restlessness to a standard (uncomfortable) stimulus than it did before having the drug. If abstinence irritability gradually increases, the longer the animal is given the drug, the animal is considered to be becoming "physiologically dependent" upon the drug: he can remain comfortable and have a relative degree of functional normality only if he continues to take the drug regularly. Rather than experience the uncomfortable withdrawal effects, the physiologically dependent animal will then manifest his "addiction" by taking more of the drug if he can find it.

There is, in the literature, contrary experimental work with animals concerning the addiction properties of barbiturates. Seevers and Tatum[4] administered sodium barbital to dogs, daily, for months or years —until the dogs died. The dosage was approximately 100 mgm/kgm of body weight. Our use of sodium amytal, 60 grains per day, represents a dose of 60 mgm/kgm in a patient weighing 147 pounds. The established clinical dosage of sodium barbital to humans is 5 grains; that of sodium amytal, 3 grains—a ratio of 5:3. Therefore our dose of 60 mgm/kgm of sodium amytal to humans is very similar to their dose of 100 mgm/kgm of sodium barbital to dogs. The description they give of their dogs is so similar to our observations on humans that I wish to quote at some length: "When receiving the dosage regularly, the animals were always apathetic and not acutely aware of their surroundings, even though walking about and taking nourishment. Within a period of 2 to 6 months, depending on the severity of the poisoning, characteristic physical signs appeared. These were seen best 24 hours following the last dose of the drug. Muscle tremors, incoordinate gait, and a type of intention tremor seen when the animal attempts to take food, are the predominant signs. These signs disappear after the daily dose is given and when the animal arouses from his period of sleep, he is quite normal except for his apathy. If the dog is allowed to go 48 hours without any barbital, nervous irritability increases, the tremors become more severe, motor unrest with continuous ataxic movement is seen. Convulsions were seen frequently." Seevers and Tatum refer also to the work of certain German authors (Hoff and Kauders) working in 1926, who had made similar observations. "Their animals became progressively more irritable and were ataxic and incoordinate. They were fairly normal when aroused from sleep, but after 24 hours of abstinence were wild and attempted to bite." Hoff and Kauders, according to Seevers and Tatum, also had observed convulsions in the dogs, clonic tremor, and shortening of the sleeping time even though the dose of the drug was increasing. Seevers and Tatum concluded that sodium barbital causes physiological dependence: "Thus barbital fits in

the category of those drugs which after long use require a continuance of the drug to maintain a certain degree of functional normality."

Stanton[5] and Swanson[6] reached an opposite conclusion. Stanton tested rats for abstinence irritability, with doses of phenobarbital and pentobarbital up to 30% minimum lethal dose daily for seven weeks. His largest dose of sodium pentobarbital was 36 mgm/kgm of body weight. Assuming an "equivalent dose" ratio of 1½:3:5 for sodium pentobarbital, sodium amytal, and sodium barbital respectively, based on clinical practice, his dose of barbiturate was slightly more intensive than that which we use (i.e., as 72:60) and which Seevers and Tatum used (i.e., as 120:100). Nevertheless, he failed to find an increase in abstinence irritability, and therefore concluded that these drugs do not have an addiction liability. Swanson did a similar experiment with dogs and monkeys, administering sodium amytal three times a week, for three to six months. His dose was 40 mgm/kgm, which (on the "equivalent dose" ratio of 3:5) is only about 2/3 as intensive (i.e., as 67/100) as the dosage of sodium barbital Seevers and Tatum gave their dogs. Swanson's animals showed no abnormal symptoms when the drug was discontinued, and he therefore also concluded that sodium amytal did not have addiction properties.

These contrary conclusions might be explained by assuming that different drugs of the barbiturate class have markedly different withdrawal effects, or by assuming that different species of animals have markedly different reactions to abstinence from the barbiturates. There is some truth in those assumptions, but I do not believe they are the complete answer. For example, Swanson's work with sodium amytal is contrary to our experience with the same drug. Swanson's results with dogs are contrary to the work of Seevers and Tatum with dogs. A better explanation of the difference seems to be that there are degrees of severity of withdrawal effect. The slightest degree is probably subjective discomfort—which is not easily detected in laboratory animals, but is certainly an important factor in clinical drug addiction. A greater degree would be observed in abstinence irritability—an increased response to a constant stimulus. A still greater degree would appear in objective signs, such as tremor and ataxia, without a special stimulus. The severity of withdrawal effects (with regard to a certain specific drug), is in turn related to three factors: The size of the dose, the time interval between doses, and the duration of administration of the drug. Swanson gave a barbiturate three times a week, and observed no objective signs of withdrawal effect; Seevers and Tatum gave 50% more, and gave it daily, and observed signs in two to six months. We also give 50% more than Swanson, but give it around-the-clock, keeping the patient continuously narcotized, and cause those signs in 10 days or less.

The abstinence symptoms we cause in our patients (by about 60 grains of sodium amytal per day, in divided doses, for about 10 days) are so severe that a patient would gladly welcome more of the drug as an immediate relief from the symptoms. However, we cannot assume we have proved that sodium amytal has significant addiction properties, in dosages ordinarily encountered clinically. But it seems equally incorrect to assume, on the basis of Stanton's and of Swanson's work with animals, that barbiturates have *no* tendency to cause an addiction based on withdrawal effect. The truth lies somewhere in between.

Barbiturates can cause some withdrawal effects, and therefore have some tendency to cause physiological addiction. Large doses cause severe subjective and objective withdrawal effects. Lesser doses—which may not cause objective withdrawal effect in a laboratory animal—may still be sufficient to cause some subjectively uncomfortable withdrawal effects.

Subjective discomfort is an important factor in human drug addiction. Since we cannot readily separate, in a human, those uncomfortable feelings which are due to drug abstinence, and those which are due to intrapsychic conflicts, it is reasonable to try to measure the addiction liability of a drug by its ability to cause observable abstinence symptoms in a laboratory animal. However, this is too indirect to permit exact

transposition of the results from the laboratory to the clinical field.

Clinical experience strengthens the above opinion, that barbiturates do cause some withdrawal effects, in dosages encountered clinically, as well as in the unusual dosages we use in the sodium amytal narcosis therapy. I will cite briefly several clinical illustrations. It is well known that an epileptic, suddenly removed from his drug, is likely to have an increase in seizures beyond his "normal" frequency. I recently observed a woman in an anxiety state, who had been taking about 20 grains of sodium amytal a day, in divided doses. When this was discontinued, she experienced about three days of sleeplessness, tremor, emotional disorganization, and ataxia. These symptoms then vanished, but there was still disturbed sleep, tremor, and emotional instability based on the anxiety state. These were of a lesser degree, and even qualitatively different, than the earlier symptoms, which I attributed to abstinence from the sodium amytal.

I have observed several cases of chronic psychoneurosis, which have been taking about three or four times the average dose of some barbiturate for months or years for insomnia. Regularly, if they discontinue the drug, these patients experience about 72 hours of absolute sleeplessness and severe subjective discomfort. The symptoms which remain, due to the psychoneurosis, may be very similar, but are quantitatively less, after that initial period of abstinence from their accustomed drug.

Finally, I will cite the case of a pregnant woman with hypomania, who took 40 grains of sodium barbital daily for several months, until she delivered her child. The drug was then abruptly discontinued, and the patient, who had never had signs or symptoms of epilepsy, had a major convulsion 48 hours later.

"Withdrawal effect," or "toxic effect?" Stanton was acquainted with the work of Seevers and Tatum, but did not accept their conclusions about physiological dependence. Instead, he interpreted the symptoms produced as being due to the direct cumulative action of the barbiturates. This interpretation was facilitated by Seevers and Tatum using the word "poisoning" to describe their method of administration of the drug. Furthermore, Seevers and Tatum carried on the administration of the drug until the dogs died, and then were able to demonstrate in the brains chronic parenchymatous and chronic interstitial injury. The symptoms we are considering cannot be related to those pathological changes directly, for symptoms based on cell death would not be reversible, in three or four days, as these are. But since the entire procedure does lead, in the end, to death of brain cells and death of the animal, the sickness of the animal—the symptoms we interpret as withdrawal effects—might well represent "sickness" or "toxicity" of brain cells. Assuming this is so, is this sickness, or malfunction of brain cells due at the moment to too much or to too little barbiturate being present in the body? Is the "toxic" agent, at the moment, barbiturate, or some other agent which the barbiturate can counteract? Are the symptoms the "direct" and "cumulative" effect of barbiturate, or are they evidence of "withdrawal effect"? I believe these questions are answered by the fact that usually more barbiturate relieves the symptoms. In an occasional instance when the "toxicity" has seemed to be of dangerous degree, particularly because of more than three convulsions, we have used sodium phenobarbital.

We do not deny that the sodium amytal narcosis treatment probably results in the death of some brain cells, but there have been no clinical signs after the treatment to give that theoretical presumption practical significance. As long as the general therapeutic results are good, the method has merit, just as other "destructive" procedures, such as prefrontal lobotomy, are justified by the therapeutic result.

"Counter-adaptation." Sickness, or toxicity, of the brain cells has been produced by the administration of barbiturate; but the toxic agent, at the moment, seems to be, not barbiturate, but some other agent which barbiturates can counteract. This phenomenon becomes easy to understand with the acceptance of the idea of counter-adaptation advanced by Schutz. He found that prolonged administration of barbiturates greatly reduced cholinesterase activity of

the serum so that it reached 10 to 20% of what it was before the drug was given. No change in cholinesterase activity was found when the drug was added to the serum in vitro. Thus, the barbiturates do not appear to act directly on enzymes, as in the case of anticholinesterase substances. The decrease in cholinesterase is an in vivo adaptation of the body to the presence of the barbiturate. Exactly how the body effects this decrease is a biochemical problem I am not qualified to discuss.

The idea of counter-adaptation clarifies these problems of drug addiction. The administration of a given drug has a given direct effect, in the case of barbiturates, inhibition of the function of certain nerve cells. But a second, indirect effect, a counter-adaptation designed to defend the cell, also begins. The counter-adaptation, although defensive is equally unphysiological. In order to maintain a balance which has been upset by the barbiturate in the direction of inhibition, its effect is an unphysiological excitation. The balance is then precariously maintained. The counter-adaptation proceeds somewhat more slowly than the direct effect, but also wears off more slowly than the drug is excreted. Therefore, it is present in the body to counteract the next dose of drug and reduce its direct effect. This is the phenomenon we know as "tolerance" to a drug. As the dose of the drug increases, the degree of counter-adaptation increases. At a certain point, the unphysiological excitation effects of the counter-adaptation begin to be obvious a few hours after the last dose of the drug, and so more drug is required to maintain the functional balance. This is the phenomenon we know as "physiological dependence." If more of the drug is not given, the unopposed effect of the counter-adaptation is clearly seen. The patient experiences the symptoms we know as "abstinence irritability" or "withdrawal effects."

The biochemical counter-adaptation to barbiturates is particularly intriguing because the symptoms it causes (restlessness, insomnia, tremor, feeling of tension, and psychic phenomena) are so similar to those which result from psychogenic conflict—which must also, in the last analysis, be a biochemical process.

Significance

The above discussion has practical significance in these areas: The matter of convulsions; the matter of barbiturate addiction; and the matter of barbiturate psychosis.

Convulsions: It is well known that an epileptic suddenly discontinuing his anticonvulsant drug may have more frequent seizures, or even status epilepticus. It is not so well known that barbiturate addicts, who are not epileptic, may have convulsions if their barbiturate is suddenly stopped. Curran,[8,9] discussing barbiturate psychosis, states that convulsions occurred in 10% of his patients. Cecil's Textbook of Medicine[10] also mentions the probability of convulsions in "advanced cases" of "overdosage" of barbiturates. Neither of these makes it specifically clear that the convulsions come from withdrawal of barbiturate, and that the immediate treatment to control the convulsions would be more barbiturate rather than less. Also, these are rather isolated references to the occurrence of convulsions through misuse of and withdrawal of barbiturates. For example, Goodman and Gilman's Textbook of Pharmacology[11] does not mention the fact.

We suggest that, in treating severe barbiturate addiction, the barbiturate be withdrawn gradually by halving the dose each day, in order to avoid the possibility of convulsions. These convulsions are severe and have, in our experience, caused compression fractures of the vertebrae similar to those seen following electroshock convulsions.

Addiction: Cecil states that "discontinuance of the use does not result in physiologic manifestations of addiction." Curran states, "a discontinuance of the use of the barbituric acid compounds does not give rise to a series of symptoms indicative of the body having developed a physiologic dependence on the drug." These opinions are apparently based in part on the animal experiments of Stanton and of Swanson which I have discussed previously. I wish to repeat the conclusion expressed in that discussion, that barbiturates do, under the unusual dos-

ages of the sodium amytal narcosis, produce unmistakable signs of marked physiologic dependence. It is my impression in ordinary clinical experience that similar, though much milder symptoms of physiologic dependence occur from the misuse of barbiturates. Since the symptoms are mild requiring no special treatment, and lasting only two or three days, they may readily pass unnoticed, being dismissed by the doctor as symptoms of the underlying psychoneurosis for which the barbiturates were originally prescribed. Before the degree of discomfort due to psychogenic factors can be accurately assessed, the patient has about three days of uncomfortable withdrawal symptoms. If the doctor does not know that, he may by continuing to prescribe barbiturates, miss the opportunity to deal directly with the psychoneurosis.

Barbiturate psychosis: Curran and Cecil both make the specific statement that delirium due to barbiturates is "rare." Curran describes the psychotic picture as being usually euphoric. However, he does point out that "on the other hand, irritability, agitation, and depression are occasionally seen." I have no reason to differ with his description of psychoses induced by indiscriminate use of barbiturate, as they are seen clinically; but I do have reason to know that delirium (hallucinations, tremor, insomnia) can be induced in a very few days by heavy, continual dosages of sodium amytal. Furthermore, in the "psychotic" state our patients exhibit for a few days after the narcotic phase, there is no common pattern to the mental content. The delirium is constant, but the mental content reflects the psychiatric condition for which we administered the treatment. I therefore suggest that in the cases of barbiturate psychosis which will be seen clinically, the psychiatric symptomatology will depend more upon the psychiatric condition which led the patient to take barbiturate unwisely, than upon the specific effect of the barbiturate.

Summary

1. A description is given of the symptoms (hallucinations, tremor, insomnia, and occasionally convulsions) which follow the abrupt discontinuing of sodium amytal for about 72 hours after its constant presence in the body for about ten days (about 60 grains per day).

2. These symptoms are interpreted as withdrawal effects, and as an indication that sodium amytal in that dosage creates severe physiological dependence.

3. These observations force the conclusion that some physiological dependence on barbiturates occurs in dosages which are not uncommon in ordinary clinical practice; and that the doctor's accurate evaluation of the underlying psychoneurosis may be obscured by the symptoms of abstinence from the barbiturates.

4. The theory of biochemical counter-adaptation to explain physiological dependence is advocated.

5. The relation of these observations to the clinical problems of convulsions in drug addicts, of barbiturate addiction, and of barbiturate psychosis is discussed.

REFERENCES

1. Heldt, T. J.: Therapeutic Use of Prolonged Sodium Amytal Narcosis. *Am. J. Psychiat.*, 104: 27-35, 1947.
2. Palmer, H. D., and Paine, A. L.: Prolonged Narcosis as Therapy in Psychoses. *Am. J. Psychiat.* 12: 143-164, 1932.
3. Palmer, H. D., and Braceland, F. J.: Six Years' Experience with Narcosis Therapy in Psychiatry. *Am. J. Psychiat.*, 94: 37-53, 1937.
4. Seevers, M. H., and Tatum, A. L.: Chronic Experimental Barbital Poisoning. *J. Pharmacol. and Exper. Therap.* 42: 217-231, 1931.
5. Stanton, E. J.: Addiction and Tolerance to Barbiturates. *J. Pharmacol. and Exper. Therap.*, 57: 245-252, 1936.
6. Swanson, E. E., Weaver, H. M., and Chen, K. K.: Repeated Administration of Amytal. *Am. J. M. Sc.*, 193: 246-251, 1937.
7. Schutz, F.: Mechanism of Drug Addiction and Drug Tolerance. *Nature*, 148: 725-739, 1941.
8. Curran, F. J.: Current Views on Neuropsychiatric Effects of Barbiturates and Bromides. *J. N. & Ment.*, 100: 142-169, 1944.
9. Curran, F. J.: Symptoms and Treatment of Barbiturate Intoxication and Psychosis. *Am. J. Psychiat.*, 95: 73-83, 1938.
10. Cecil: Textbook of Medicine, 7th Edition, page 599. Philadelphia, *W. B. Saunders Co.*, 1947.
11. Goodman and Gilman: Pharmacological Basis of Therapeutics, page 141. New York, *MacMillan Co.*, 1941.

Dramamine In the Prevention and Treatment of Nausea and Vomiting Following Electroshock Therapy

EDWARD F. KERMAN, M.D.
Baltimore, Maryland

This report deals with the efficacy of dramamine in the prevention and treatment of nausea and vomiting following the administration of electroshock therapy. These unpleasant symptoms are commonly observed to occur in about twenty per cent of patients who receive this form of therapy.

It is important to prevent this seemingly minor complication for two reasons. In the first place, there is the possibility of lung abscess or aspiration pneumonia if the patient vomits while in a state of unconsciousness induced by electroshock. Secondly, one may anticipate better cooperation from the patient in continuing his treatments if the unpleasantness of nausea and vomiting is avoided.

Concerning the matter of lung abscess, Kwalwasser et al[1] have recently reported on a series of 2562 patients treated with approximately 50,000 electroshock treatments in which the incidence of lung abscess was approximately one per cent. Kalinowsky and Hoch[2] speak of the "apparent absence of such pulmonary complications in ECT." In my own experience with the treatment of 1472 patients in office practice, I have had one case of lung abscess.

The question of etiology of pulmonary abscess is relevant to our present discussion and special inquiry is here directed as to the role of aspiration in its formation. Kalinowsky and Hoch[2] state, "The development of pulmonary diseases during treatment is rare in ECT but was quite frequent in metrazol therapy. Pulmonary abscess and gangrene were originally explained as due to aspiration of foreign bodies or septic material while the cough reflex is absent, or by direct action of metrazol on lung tissue.[3] Another explanation is the formation and later mobilization of thrombi on the site of the metrazol injection.[4,5] The apparent absence of such pulmonary complications in ECT makes this explanation quite probable. Pulmonary embolism from pelvic thrombosis has also been observed. The literature on ECT contains only one case of pulmonary abscess, which might have been accidental.[6] Bronchopneumonia likewise is not infrequent in metrazol therapy and is usually described as aspiration pneumonia." From the foregoing, therefore, it may be concluded that Kalinowsky and Hoch consider the likelihood but do not place too much emphasis on the possibility of aspiration as a cause of lung abscess following the administration of electroshock therapy.

Kwalwasser et al,[1] on the other hand, commenting on the etiology of these abscesses, state, "From a surgical standpoint, the location of the abscesses is worthy of note with the predominant number located in the upper lobes and in the right lung. It is generally stated that the lower lobes are likely to be involved. However, the work of Brock[7] and others show that aspiration in the supine position does involve the upper lobes more frequently, particularly on the right. He cites evidence that lipiodol injected into the nose while the person is asleep wil be aspirated into the lungs, particularly the upper right lobe. This seems to us to be the most logical explanation for the etiologic mechanism of lung abscess in electroshock therapy."

In the past I have used numerous drugs in an effort to prevent and treat nausea and vomiting associated with treatment. Antispasmodics such as trasentine and pavatrine, belladonna preparations and atropine were used with absolutely no success. Various barbiturates were tried as premedication in cases where nausea was known regularly to follow treatment and were also unsuccessful. Amphetamine sulfate was found to be unavailing in producing any benefit.

It occurred to me, following the work of Gay and Carliner,[8] that dramamine might be used profitably in those patients who experience the gastrointestinal discomfort under discussion. It seemed well to lay major emphasis on premedication rather than to

try to use the drug in the treatment of established nausea since in the latter case the patient might not retain the orally administered medication.

I have treated fifty-five patients receiving electroshock therapy with dramamine. My usual procedure is as follows: The patient is instructed routinely to take nothing by mouth for three hours before the treatment. If he awakens after his first electroshock and complains of nausea, or if he vomits, he is given 100 mg. of dramamine at that time. If he is able to retain the drug he usually experiences relief in from fifteen to twenty minutes. Since it is known that patients who show nausea with one treatment usually do so with subsequent ones, one then attempts to prevent its appearance in future treatments by prescribing dramamine as premedication. The patient is instructed to take 100 mg. of the drug one hour before the scheduled treatment.

Of the fifty-five patients comprising this study there has been complete prevention or relief of nausea and vomiting in fifty-one. Three patients experienced some nausea but not as marked as they had without dramamine. In only one case was the drug considered a failure. These results (93% complete prevention or relief and 98% benefited) are strikingly similar to those reported by Gay and Carliner[8] who claimed complete relief from motion sickness in 288 out of 300 subjects or 96%.

One patient in my series, because the change was so dramatic, merits special comment. She received forty nine shock treatments in two courses, one in 1948, the other in 1949. Up until May 31, 1949 she had been given forty electroshocks and had vomited violently after each. On the date mentioned she was given dramamine one hour before her treatment. On awakening from electroshock she was carefully questioned and denied even the existence of nausea. The rest of her treatments, given with dramamine premedication, were taken without the appearance of the usual gastrointestinal upset. I felt that this was a particularly significant response since the prevention of vomiting in this patient could hardly be considered coincidental.

My experience with dramamine in the prevention and treatment of post-shock nausea and vomiting led me to an interesting bypath. This experience, along with my preliminary report of the present study, was published in the correspondence section of the Journal of the American Medical Association.[9] I gave one of my patients a prescription for dramamine to prevent her nausea following electroshock. One day, shortly thereafter, her father told me that he had an attack of migraine from which illness he had been suffering a long time. In view of the fact that he experienced nausea with his headache he decided to try one of his daughter's tablets. He claimed that the migraine attack was aborted by the medication.

Folowing this, I gave the drug to seven other patients suffering from migraine and in every case I was advised by the patient that it was effective and I commented on this in my preliminary report.[9] Since then, my subsequent experience with dramamine in the treatment of migraine has not been as good. All told, I have treated twenty patients. In about half of this series benefit was either absent or equivocal. In the remaining half, relief from migraine has been obtained at times and not at others even though the drug was always taken at the very onset of the attack. Concerning the original eight patients described in my preliminary report, further use of dramamine indicated that it was effective on some occasions but, in general, relief was not consistent. I have concluded that dramamine may be helpful in some cases of migraine, especially if taken early in the course of an attack, but that its value probably depends on its sedative rather than specific action. I am strongly impressed with the fact that dramamine cannot be considered as specific as ergotamine tartrate which still remains, in my opinion, the most reliable agent to abort an attack of migraine. My ultimate findings, then, with regard to the use of dramamine in the treatment of migraine do not coincide with those of Brentan[10] who claims that by using dramamine at the onset of prodromal symptoms all of his seven patients responded to the medication by abortion of all of the manifestations of the migrainous headaches and were able to resume normal activities almost immediately. I sus-

pect that as Brentan continues his study, as I did, his subsequent results will be less encouraging than his original ones.

Comment

It is essentially the purpose of this report to publish the fact that a highly effective therapeutic agent exists in the form of dramamine to prevent or relieve nausea and vomiting following electroshock therapy. It is quite natural, however, to ask ourselves the question of its mode of action and from this, possibly, to speculate on the nature of the production of post-shock nausea.

As in the case of motion sickness, we observe in our patients the symptoms of pallor, cold sweating, increased salivation, nausea and vomiting.[11] Similarly, we observe that in about the same high percentage of cases as reported for motion sickness[8] we obtain relief from these symptoms in our patients by the use of dramamine. It does not appear unreasonable to assume that vestibular stimulation, considered responsible for motion sickness,[11] is similarly causative of the symptoms of post-shock nausea. Such stimulation might either be induced by the convulsive movements during treatment or, more likely when one considers the site of electrode placement, by direct electrical stimulation of the vestibular system. Since dramamine appears to exert its effects "by acting both upon the vestibular end-organ and the nerve tract, peripherally or centrally"[12] and since it exerts very little specific action on the blood vessels, it is not surprising that its effect on the symptoms of migraine is an inconsistent one. We may therefore conclude, from our clinical observation of the results herein reported, that it appears likely that the symptom complex of nausea and vomiting following electroshock therapy results from vestibular stimulation in individually predisposed patients and that dramamine acts in preventing or relieving these symptoms in a manner similar to that which it exerts on motion sickness.

Summary

Fifty-five patients treated with electroshock who experienced nausea and vomiting following their treatment were given 100 mg. of dramamine by mouth. This was generally administered to these patients, once their predisposition to this complication was determined, one hour before shock therapy. In a few instances the drug was administered to relieve established nausea. Fifty-one patients (93%) experienced complete prevention or relief. Three patients reacted to medication with a diminution in the severity of the nausea. In only one case was the drug considered a failure. It is suggested that post-shock nausea is caused by vestibular stimulation occurring during the course of electroshock therapy and that the mode of action of dramamine upon it is similar to that which it exerts in motion sickness.

3700 LIBERTY HEIGHTS AVE.

REFERENCES

1. Kwalwasser, S., Monroe, R. R., and Neander, J. F.: Lung abscess as a complication of electroshock therapy. *Am. J. Psychiat.* 106: 750-754, 1950.
2. Kalinowsky, L. B., and Hoch, P. H.: Shock treatments and other somatic procedures in psychiatry. *Grune & Stratton,* New York, 1946.
3. Gianelli, V., and Sani, C.: Sur la therapeutique convulsante de la schizophrenie et d'autres maladies mentales par le cardiazol. *Schweiz. Arch. f. Neurol. u. Psychiat.* 49: 92, 1942. Quoted by (2).
4. Beckenstein, N.: Results of metrazol therapy in schizophrenia. *Psychiat. Quart.* 13: 106, 1939. Quoted by (2).
5. Zeifert, M.: Etiology and prevention of "lung abscess" in metrazol therapy. *Psychiat. Quart.* 13: 303, 1939. Quoted by (2).
6. Kalinowsky, L. H., and Worthing, H. J.: Results with electric convulsive treatment in 200 cases of schizophrenia. *Psychiat. Quart.* 17: 144, 1943. Quoted by (2).
7. Brock, R. C.: The anatomy of the bronchial tree. *Oxford University Press,* N. Y. 1946. Quoted by (1).
8. Gay, L. N., and Carliner, P. E.: The prevention and treatment of motion sickness. *Bull. Johns Hopkins Hosp.* 84: 470, 1949.
9. Kerman, E. F.: Dramamine for nausea of electric shock and migraine. *J.A.M.A.* 141: 478, 1949.
10. Brentan, E.: Treatment of migraine with dramamine. *Rocky Mountain M.J.* 47: 197, 1950.
11. Tyler, D. B., and Bard, P.: Motion sickness. *Physiol. Rev.* 29: 311-369, 1949.
12. Gutner, L. B., Gould, W. J., and Batterman, R. C.: Studies on pharmacology of dramamine. *Federation Proceedings.* March 1950. Vol. I, No. 1 (pages 3-400).

Paget's Disease Complicated By Recurrent Extradural Hematoma

WILLIAM G. PEACHER, M.D.
Syracuse, New York

No more descriptive term has been given of Paget's disease than the one by James Paget himself when he wrote, "Holding, then, the disease to be an inflammation of bones, I would suggest that, for brief reference, and for the present, it may be called, after its most striking character, osteitis deformans. A better name may be given when more is known of it." (James Paget.[1])

The man in whose honor the disease was named was one of the first to direct attention to this entity. His description of five cases, two of which were autopsied, could not be improved upon today. Paget further states, "Even when the skull is hugely thickened, and all its bones exceedingly altered in structure, the mind remains unaffected." Subsequent clinical studies in this respect, however, have demonstrated occasional mental and numerous other neurological implications.

We recently had the opportunity to study a very interesting and most unusual case of Paget's disease complicated by recurrent extradural hematoma. Considering the relative frequency of involvement of the skull in this disease, together with the type of pathology present, it is surprising that this sequela is not more commonly observed. This case is being presented in detail due to its rarity and also to illustrate the problems it presented in management.

Case History

At the request of Dr. Herbert Yeckel, I.G., a seventy-four year old female, was first examined September 28, 1948 with a chief complaint of gradual and progressive enlargement of the left parietal bone of at least four years duration. The patient was more concerned about her cosmetic appearance and her inability to wear a hat than the more obvious pathological features. Aspiration of this large mass previously had yielded a grossly bloody fluid, and the patient had been referred for neurosurgical intervention due to the possibility of complicating sarcoma.

The physical examination revealed findings typical of Paget's disease. The cranium was greatly enlarged with general thickening of the bone. The scalp vessels were prominent particularly over both frontal and left parietal areas. The increase in size of the skull was most apparent over the left frontal and parietal bones at the site of which there was a large, ovoid, non-tender, non-inflammatory, soft, boggy, fluctuant mass measuring approximately 8.75 x 8.75 x 5 cm. in diameter. There was considerable thinning of the scalp to the point of rupture. Several small fragments of detached bone could be palpated beneath the margins of the defect. There was felt to be definite clinical evidence of extradural hematoma with sarcomatous degeneration. It is interesting to note that during hospitalization for a fracture of the left femur in July, 1945, although x-rays of the skull were not taken, definite enlargement of the left parietal bone was noted together with general asymmetry of the skull.

The physical examination further revealed bossing and irregularity of the squamous portions of the frontal bone but no change in the bones of the face. The long bones of the lower extremities were quite massive with a genu valgum on the right, and deformity of the left thigh due to a pathological fracture of the left femur sustained July, 1945. Similar bowing, irregularity, and lateral curvature were noted of both bones of either forearm, more evident on the right. A moderate dorsal kyphosis was also present. Although the blood pressure was normal, sclerosis of the peripheral and fundal vessels was present. In spite of the multiple deformities, the patient was ambulatory and could take care of her simple household needs. The only limitations were in relation to impairment of memory, comprehension, and hearing.

Considering the probable extreme degree of cortical compression, the neurological examination was not unusual. The main findings were marked impairment of memory and attention which was felt to be due to associated arteriosclerosis as well as cerebral pressure from extradural hematoma. Perceptual implication in the visual and auditory fields was also evident.

Laboratory findings: Blood count, urinalysis, and serology were negative. Sedimentation rate was 24 mm. in one hour. Serum calcium: 8; serum phosphatase: 2.6; alkaline phosphatase: 13 Bodansky units. X-rays of the skull taken August 23, 1948 revealed typical findings of osteitis deformans of the bi-phasic type involving all bones of the vault. The process was most extensive over the left parietal bone where bone destruction predominated. A large, soft tissue mass was seen extending from the latter area (see Fig. 1).

The patient was accordingly admitted to St. Joseph's Hospital, Syracuse, New York, October 5, 1948 for further observation and treatment. A left central craniotomy was performed October 6, 1948

Fig. 1.

outlining the extensive soft tissue mass over the involved parietal bone. As the periosteal layer was reflected numerous, small, detached, degenerated fragments of bone were observed throughout the outer layers of the mass. The main structure was found to consist of many, irregularly loculated cavities of varying size filled with old and recent blood. There was considerable depression of the entire left cerebral hemisphere to a depth of at least 5 cm. in the field at hand. The dura was ragged and irregular along the course of the middle meningeal vessels but no gross invasion was manifest. There was tremendous hypertrophy (up to 2-3 cm.), degeneration, and increased vascularity of the diploe. Representative sections of tissue were sent for analysis to rule out malignancy. It was only after great difficulty that hemostasis was secured by means of coagulation, bone wax, pressure, and gelfoam. The vascularity, thinness of bone, manipulation necessary, prolongation of the procedure, age, and possibility of recurrence and progression of the disease obviated insertion of a tantalum plate at this time. The patient made an uneventful convalescence, and the wound healed by primary union. Microscopic sections revealed active Paget's disease with no evidence of malignancy. The patient was discharged improved on October 19, 1948.

The patient did very well for about a month and then noted gradual reaccumulation of fluid at the previous site of involvement. The neurological and physical features were identical with those recorded previously (see Fig. 2).

She was therefore readmitted to the hospital on December 5, 1948 and operated on December 6, 1948. Similar findings were determined at this procedure. Again there was subsidence of bleeding but the patient's hospitalization was purposely prolonged for early control of possible recurrence. Unfortunately such proved to be the case, and the third craniotomy was performed January 8, 1949. The possibility of angiography to determine the source of maximum bleeding for more effective ligation was discussed with the family. They were also informed of the risks of angiography at this age due to the patient's marked cerebral arteriosclerosis which with possible vasospasm from diodrast could result in hazardous neurological consequences as well as the sequelae of common and internal carotid section (in the dominant hemisphere). The relatives decided against the procedure but consented to external carotid artery ligation which was accordingly done.

The patient did reasonably well following this operation although there was increasing mental hebetude and confusion with interference with the dressing and onset of wound infection. Smear of the wound revealed a moderate number of gram positive bacilli and a few gram positive cocci. A culture showed staphyloccus aureus and a member of the diphtheroid group. With the increased vascularity concomitant to the wound infection, further slight but continued bleeding ensued. There

Fig. 2.

was some response to antibiotics and to the usual conservative therapy, and the patient was discharged January 21, 1949.

The patient returned sporadically for dressings, and arrangements were made for a visiting nurse to see her daily. Hospitalization became necessary

for more active therapy from February 14 to February 23, 1949. On her discharge which had been at her insistence, she became increasingly uncooperative and mentally incompetent necessitating total care. Her final entry to the hospital was made on April 8, 1949. Slight sanguino-purulent drainage had continued from the wound since her discharge from the hospital January 21, 1949 in spite of adequate conservative therapy. This, together with her greatly depraved condition and in spite of slight continued bleeding, obviated further attempts at surgical correction. The patient gradually went downhill expiring on June 1, 1949. Unfortunately, permission for post-mortem examination was not granted.

Discussion

Numerous statistical studies have appeared in the literature on osteitis deformans. The incidence, subjective manifestations, osseous implication, laboratory and x-ray findings, pathology, complications and therapy have all been adequately reviewed by Newman,[2] Sugarbaker,[3] Kay,[4] Gutman and Kasabach,[5] Reifenstein and Albright,[6] Sosman,[7] Orley,[8] and Kasabach and Dyke.[9]

Many excellent reviews have been written on the incidence of sarcomatous degeneration in Paget's disease.[10,11,12,13] These figures have varied from two to four percent. Certainly this possibility must be considered in the management of every case. Although it was felt that our patient undoubtedly had a lesion of this type clinically, subsequent microscopic sections were entirely negative.

Further evidence of the possible dangers of diodrast in relation to neurological complications as a result of vasospasm following arterial injection was reported by Chusid, Robinson, and Margules-Lavergne.[14] They presented two cases of hemiplegia due to vasospasm following the injection of diodrast before the New York Society of Neurosurgeons. Recovery was effected following the administration of tetraethylammonium chloride. During the general discussion following their presentation, twenty-one additional cases with similar complications were mentioned. The factor of recovery was not included in this summary.

Alpers[15] states that neurological symptoms associated with Paget's disease are commonly due to:

1. Constriction of the cranial foramina.
2. Distortion of the skull with intracranial compression.
3. Associated cerebral arteriosclerosis.

The nervous system may be implicated in the following ways:

Central Nervous System:

1. Psychoses. This complication is regarded as being uncommon and secondary to arteriosclerotic atrophy or increased intracranial pressure.[16,17,18]
2. Increased intracranial pressure.[19,20]
3. Focal neurological signs, e.g., hemiplegia, dysphasia, etc. Basilar impression with hind brain symptoms is not rare according to Grunthal,[21] Chamberlin,[22] and Wycis.[23] Decompression has given relief in selected instances in this group.

Spinal Cord Syndromes:

1. Compressive with varying degrees of neurological dysfunction most common at the thoracic level.
2. Vascular impairment secondary to compression with cord symptoms. Therapy for intractable pain due to nerve root compression may be necessary.
3. Vertebral dislocation. An occasional case is associated with hematomyelia.

The literature on spinal cord involvement has been adequately reviewed by Wyllie,[24] and Turner.[25]

We recently observed a case which falls in this group. A seventy-four year old male noted the gradual onset of motor and sensory implication of the lower extremities over a period of one month. When referred for neurological examination January 13, 1950 a spastic paraplegia with a sensory level at dorsal seven was present. X-rays of the dorsal spine on January 9, 1950 had revealed extensive osteo-arthritic changes of the lower thoracic vertebrae. A lumbar puncture was performed on January 10, 1950. The significant findings were an elevated total protein (400) and a block on jugular compression. These data were corroborated on pantopaque myelography January 16, 1950 which demonstrated an almost complete obstruction at dorsal five. All other laboratory procedures were negative, and there was no evidence of either axial or appendicular Paget's disease. A dorsal laminectomy was carried out on January 17, 1950, the delay being due to indecision of the family in giving consent for the operation. Some hypertrophy, degeneration, and increased vascularity of the spinous processes and laminae at dorsal four, five, and

six were noted. The bone at dorsal five also appeared to be involved in a more soft, friable, reddish-brown type of lesion. Dural pulsation was not present until decompression had been completed from dorsal three through seven. The pathological report revealed osteogenic sarcoma arising on the basis of localized Paget's disease. Further deep x-ray therapy is being planned. There was no early improvement in the paraplegia postoperatively. Cases of this type are relatively rare. Further, decompressive laminectomy has occasionally resulted in improvement particularly when uncomplicated by sarcoma as demonstrated by Turner.[25]

Peripheral Nervous System:

1. Cranial nerve involvement. The optic and auditory nerves are most commonly implicated.[17, 26]
2. Peripheral nerve symptoms such as intercostal neuritis, sciatica, etc.

Summary

Surgery is occasionally necessary during the course of osteitis deformans when the central nervous system is involved. An instance of this type has been recorded with recurrent extradural hematoma. Various problems were encountered in the management of this case and may include the following considerations.

Although other primary (meningioma, osteoma, etc.) and metastatic (thyroid, etc.) lesions of the skull may produce localized hypertrophy comparable to the present case, the overall picture generally indicates the correct diagnosis.

Angiography should precede removal of the hematoma if the condition of the patient permits. Differential cannulation of the internal and external carotid arteries as well as phlebography may be necessary to determine the exact blood supply of the lesion. Such information will do much to demonstrate the presence of anastomoses and extent of arterial ligation indicated as well as to differentiate neoplastic lesions.

This procedure is not without danger, however, as diodrast may result in severe vasospasm, and together with an active carotid sinus reflex in an arteriosclerotic individual may result in cerebral thrombosis. Common carotid section may be indicated, but the risk of sequelae in this age group will be much greater. The hazards of such a procedure in this instance would probably have resulted fatally due to the poor condition of the patient. It is recommended that such ligation that is necessary precede evacuation of the hematoma as this will minimize the technical phases of the operation. Bilateral external carotid section may be indicated but should be done in stages if possible to allow for adequate anastomoses.

Tantalum cranioplasty would probably not be indicated in such cases due to possibility of recurrence of bleeding, continued progress of the disease, and technical difficulties in fixation in the presence of bone pathology of this type.

BIBLIOGRAPHY

1. Paget, J.: On a Form of Chronic Inflammation of Bones. *Medico-Chir. Transact.,* 60:37-63, 1877.
2. Newman, F. W.: Paget's Disease. *J. Bone and Joint Surg.,* 28:798-804, 1946.
3. Sugarbaker, E. D.: Osteitis Deformans (Paget's Disease of Bones). *Am. J. Surg.,* 48:414-421, 1940.
4. Kay, H. P., Simpson, S. J., and Riddoch, G.: Osteitis Deformans. *Arch. Int. Med.,* 53:208-248, 1934.
5. Gutman, A. B., and Kasabach, H.: Paget's Disease. *Am. J. Med. Sc.,* 191:361-380, 1936.
6. Reifenstein, E. C., and Albright, F.: Paget's Disease: Its Pathologic Physiology and the Importance of This in the Complications Arising from Fracture and Immobilization. *New Eng. J. Med.,* 231:343-355, 1944.
7. Sosman, M. C.: Radiology as Aid in Diagnosis of Skull and Intracranial Lesions. *Radiology,* 9: 396-404, 1927.
8. Orley, A.: Neuroradiology. Springfield, Ill.: *C. C. Thomas,* 1949, 421 pp.
9. Kasabach, H. H., and Dyke, C. G.: Osteoporosis of Circumscripta of Skull as Form of Osteitis Deformans. *Am. J. Roentgenol.,* 28:192-203, 1932.
10. Garland, L. H.: Osteogenic Sarcoma of Skull Radiology, 45:45-48, 1945.
11. Pancoast, H. K., Pendergrass, E. P.,and Schaeffer, J. P.: The Head and Neck in Roentgen Diagnosis. Springfield, Ill., *C. C. Thomas,* 1940, 976 pp.
12. Pike, M. M.: Paget's Disease with Associated Osteogenic Sarcoma, Report of Three Cases. *Arch. Surg.,* 46:750-754, 1943.
13. Summey, T. J., and Pressly, C. L.: Sarcoma Complicating Paget's Disease of Bone. *Ann. Surg.,* 123:135-153, 1945.
14. Chusid, J. G., Robinson, Franklin, Margueles-Lavergne, M. P.: Transient Hemiplegia Associated Cerebral Angiography (Diodrast). *J.N.S.,* Nov. 1946, 6:466-473.
15. Alpers, B. J.: Clinical Neurology, Philadelphia, *F. A. Davis Co.,* 1947, 797 pp.

16. Kaufman, M. R.: Psychosis in Paget's Disease. *Arch. Neurol. and Psychiat.*, 21:828-837, 1929.
17. Rabiner, A. M., and Hand, M. H.: Paget's Disease and the Central Nervous System. *N. Y. State J. Med.*, 47:2689-2694, 1947.
18. Smith, L. H.: Two Cases of Paget's Disease (Osteitis Deformans) Associated with Mental Symptoms. *J. Nerv. and Ment. Dis.*, 68:578-582, 1928.
19. John, E., and Strasser, V.: Zur Aetiologie, Klinik und Therapie der Ostitis fibrosa deformans (Paget), *Deutsche Ztschr. f. Nervenk.*, 97:81-94, 1927.
20. Moyan, R. C.: Osteitis Deformans with Psychosis; Report of Case. *Ohio State Med. J.*, 24: 206-209, 1928.
21. Grunthal, E.: The Brain in Paget's Disease of the Skull. *Ztschr. f. d. ges. Neurol. v. Psychiat.*, 136:656-675, 1931.
22. Chamberlin, W. E.: Basilar impression (platybasia); bizarre developmental anomaly of occipital bone and upper cervical spine with striking and misleading neurologic manifestations. *Yale J. Biol. and Med.*, 1939, 11:487-496.
23. Wycis, H. T.: Basilar impression (Platybasia); case secondary to advanced Paget's Disease with severe neurological manifestations; Successful Surgical Result. *J. Neurosurg.*, 1:299-305, 1944.
24. Wyllie, W. G.: The Occurrence in Osteitis Deformans of Lesions of the Central Nervous System, with a Report of Four Cases. *Brain*, 46: 336-351, 1923.
25. Turner, J. W. Q.: The Spinal Complications of Paget's Disease. *Brain*, 63:321-349, 1940.
26. Gregg, D.: Neurologic Symptoms in Osteitis Deformans (Paget's Disease), 15:613-616, 1926.

Child Admissions To A Receiving Hospital

JACK V. WALLINGA, M.D., and ARTHUR J. BACHRACH, B.S.

Cleveland, Ohio

In recent years the spotlight of psychiatric attention has been focused upon the turbulent years of childhood and adolescence. Bleuler[1] observed early that there is a markedly increased disposition to mental disease concurrent with puberty. As an important factor in the stress of adolescence, Klineberg[2] points out the conflict that exists between the child's physiological drives and the standards established by society which prevent the fulfillment of these drives. The behavioral deviations in childhood and adolescence may be generally separated into the psychoses, the neuroses, the primary behavior disorders, and the mentally defective, both with and without organic brain disease. There is still much confusion in the literature concerning the diagnosis of psychosis in children because of the early practice of making such diagnoses utilizing adult criteria. Regarding this problem, Henderson and Gillespie[3] state, "It is axiomatic that behavior which would be psychotic in an adult may be normal in a child," a truism that is particularly evident in the overly rich phantasy life of the child. They go on to say, however, that we cannot ignore, as being of no significance, the trends of behavior in childhood which might later lead to the development of a psychosis in adult life, if left uncorrected.

Among the psychoses, schizophrenia is the diagnosis most frequently made in children, with manic depressive psychosis occasionally reported, but both of these are rare until after puberty. Bradley[4] states that ". . . some psychoses of adults such as paranoia and true depression do not occur at all in children," and again,[5] "the chief functional psychosis of childhood is schizophrenia; manic depressive psychoses are of rare and questionable existence before puberty, and the other classical functional psychoses of adult life are not seen, or at least diagnosed."

The same author[6] found, in an intensive study of a group of schizophrenic and schizoid children under thirteen years of age, the following outstanding objective behavior characteristics, in order of frequency: seclusiveness, irritability when this seclusiveness was disturbed, daydreaming, bizarre behavior, diminution in number of personal interests, regressive nature of personal interests, sensitivity to comment and criticism, and physical inactivity. Blunting of affect and apathy, such as is seen in many adult schizophrenics, were not prominent in

these youngsters. The difference between the psychotic and schizoid personality was felt to be largely one of degree rather than kind, but behavior employed as an expression of individual traits, was more distorted in the psychotic children.

In differentiating psychotic from delinquent behavior, Friedlander[7] says, "A diagnosis of psychotic illness cannot be made unless other pathological symptoms are present apart from an inexplicable delinquent act." In line with this, Despert[8] observes, "Severe behavior disorders, associated with regressive characteristics, are not uncommon in young children with acute emotional disturbances. However, in the absence of affective dissociation, the diagnosis of schizophrenia cannot be made, however severe the behavior disorder."

In a discussion of conduct disorders, Van Ophuijsen[9] writes that when a conduct disturbance develops at an age beyond childhood, such as during early adolescence, he assumes that it has the significance of a psychoneurotic symptom. The late appearance in itself of a conduct disturbance in adolescence excludes the diagnosis of primary behavior disorder. Additional information indicating a personality change in a patient around puberty, a primary type of withdrawal, peculiarities which cause his parents and friends to consider him to be odd, all point toward a schizophrenic process, which, at this time, does not produce delusions and hallucinations. Aichorn[10] considers delinquency as a dynamic expression which can be attributed to the interplay of psychic forces which have created the distortion he calls "dissocial behavior," the presence of which indicates that the psychic processes determining behavior are not functioning harmoniously. When a psychic process is denied expression and the psychic energies determining it remain undischarged, a new path of discharge will be found along the line of least resistance and a new form of delinquency will result. It is even possible that a nervous symptom will develop. He also feels that dissocial behavior can result from an abnormal accumulation of affect.

In many communities the facilities for the study and treatment of children who are unable to adjust to society are inadequate, and children who are psychotic or behavior problems tend to be placed together in closed adult institutions where specific provisions for their care are not available. It is necessary, however, that in-patient facilities be established for such children, as it is often only with longitudinal study that a proper diagnosis, and subsequent therapy, can be achieved.

This study concerns a total of forty-three youngsters between the ages of nine and seventeen, inclusive, 2.3% of the total of 1901 patients admitted to Cleveland State Receiving Hospital over a period of slightly more than two years. This hospital is an institution for the observation and treatment of the acute psychoses, serving the Cleveland metropolitan area. Twenty-three of these children, or 53.5%, were admitted upon voluntary application of the parents; sixteen, or 37.2%, were sent to the hospital through the medium of the Probate Court; and the remaining four, or 9.3% of the total, were emergency admissions.

It was also found that 28, or 65.1%, of these patients were males, and 15, or 34.9%, were females, whereas the sex distribution among the adult patients for this same period was 45.1% males and 54.9% females. It is interesting to note this discrepancy between the sex ratios in the child and adult groups. Twenty-six of the children observed were of the white race, the remaining seventeen, or 39.5% of the whole group, were Negro. The Negro population of Cleveland forms 9.6% of the total. Twenty-one of the youngsters reported, or 48.8% of the group, were Protestant in religion; sixteen, or 37.2%, were Catholic; and one, or 2.3%, was Jewish. There were two who listed no religious preference, the remaining youngsters being two Amish boys and one girl who was a member of Jehovah's Witnesses.

Among those patients who had been discharged by the time this study was made, the group with the longest hospitalization was the psychotic, averaging 193 days. The group that spent the shortest time in the hospital was the behavior problem children, who remained an average of 71 days. Between these extremes were the neurotic patients who averaged 132 days and the psy-

TABLE I

Diagnosis	*Age on Admission*									*Total*	%
	9	10	11	12	13	14	15	16	17		
PSYCHOTIC										22	51.1
Schizophrenia					1	2	2	9	5	19	44.2
Manic Depressive							1		2	3	6.9
PRIMARY BEHAVIOR DISORDER	1		1		1		3	2	1	9	20.9
NEUROTIC										5	11.7
Obsessive									2	2	4.7
Hysteria				1		1				2	4.7
Anxiety State									1	1	2.3
MENTAL DEFICIENCY WITH PSYCHOSIS					1	1	3	2		7	16.3

chotic mental deficients who stayed an average of 163 days. The average stay of the entire group was 144 days.

A study of the objective behavior and overt symptoms which caused the majority of these youngsters to be brought to psychiatric attention, revealed no clear cut differences between the four main diagnostic groups. Complaints of withdrawal from normal activities, bizarre and manneristic behavior, disorientation and confusion were prevalent in the schizoid and schizophrenic children. Irritability and seclusiveness were found with equal frequency in the behavior problem and mentally deficient psychotic groups, as in the pre-psychotics. Destructiveness, temper tantrums, running away and suicidal attempts were the most frequent complaints of the group found to be primarily behavior disorders. Impulsiveness was the only outstanding characteristic of the psychotic mental deficient group, this often leading to assaultive behavior when these children were frustrated and irritated.

In Table I is presented the diagnoses of the children studied, according to their age on admission:

In the above table we see that over half of the admissions in the group were for relatively pure functional psychoses, with schizophrenia predominating and the remainder being manic depressive, manic phase. This does not necessarily mean that schizoid tendencies were not shown by these cases in earlier years in the form of withdrawal and difficulty in making a social adjustment. It is difficult to determine the accurate date of the psychotic break with reality in many adult patients, and this is even more true of children because of the varying criteria and widespread differences of opinion as to what determines a child psychosis. Childers[11] also points out that the increased social demands of the early adolescent period intensify the struggles of these children and tend to bring out a more clear cut picture of psychosis. Six children with mental deficiency became sufficiently disturbed to require hospitalization. They would fall into the group Kraepelin designated as *pfropfschizophrenie,* meaning a psychosis superimposed upon a mental deficiency. We also see that, while mental deficiency was an inherent defect, it was not until the demands of society became apparently overwhelming during adolescence, that the behavior of these children became so bizarre that hospitalization was deemed advisable.

It is interesting to note that nine of the forty-three cases, or 21%, were primary behavior disorders. Three of the group were referred to this hospital as probable psychotics after study by other childrens' agencies but prolonged observation in this hospital found them to be without psychosis. In investigating the previous social agency contact of the group of patients studied, it was found that all the patients with a final diagnosis of primary behavior disorder, after observation at this hospital, had agency contacts prior to their hospitalization. These children had either lived in an institution for a time or had been seen by an agency where psychiatric consultation was available. Eight of this diagnostic group were referred by such an agency after an aver-

age of three-and-one-half years of agency contact.

Only three of the seven psychotic mentally deficient children had a history of previous agency contacts. The others were, for the most part, brought to the hospital by their parents when they were no longer manageable at home or in their private school. Two of the neurotic children had had previous contacts neither of which had been very extensive. It was found that, among the psychotic children, twelve of the twenty-two had been seen by the social agencies before they came to Cleveland State Receiving Hospital, nine of these having had fairly prolonged contact averaging over three years. Six others had been seen by agencies immediately before referral to this hospital. There is a record of a total of fifty-nine separate agency contacts including the juvenile court system, child study homes, guidance centers, and correctional institutions. Over half of these contacts were made by the children in the primary behavior disorder group.

Twenty-seven of the forty-three children were found to have social pathology in the family background:

TABLE II

	Psychotic	Neurotic	Behavior Disorder	Mental Defective with Psychosis
Severely Neurotic Parents	1			2
Psychotic Parent	4	1	2	
Psychotic Relative or Sibling	6		2	
Mental Deficiency in Family	3	2		
Broken Homes	8	3	5	3

Here we find that broken homes was the largest single factor, being present in eight, or 36%, of the psychotic cases, in five, or 55%, of the behavior disorders, and in three each of the neurotic cases and mental defective with psychosis. Another prominent factor was the occurrence of psychosis in the family background of a number of these children, and this was found in the backgrounds of eight of the schizophrenic patients. In two of these cases, psychosis was reported in another member of the family as well as the parent. These findings suggest the influence of genetic factors in the etiology of mental illness.[12]

In the group of schizophrenic patients, electric shock therapy was used in eight of the nineteen cases. Five of these showed noticeable improvement and three remained unchanged. Insulin coma therapy was used in three cases of schizophrenia with improvement in two patients. Two of the patients receiving insulin had previously received electric shock, without a complete remission resulting. All three patients diagnosed manic depressive, manic phase, received electric shock and improved with it. It might be pointed out here that "improvement" indicates that the patient was sufficiently recovered to return to society. One of the obsessive neuroses received electric shock therapy with improvement, while another did not benefit by it. Two mental deficients with psychosis were given electric shock with sufficient improvement that made possible their return to their family's care. Five patients received intensive psychotherapy without other forms of treatment while in the hospital. Four of these children were behavior disorders, of which three showed marked improvement, and the remaining one was an hysterical child who was similarly helped. Thirty of the forty-three cases studied had been discharged at the time of writing, twenty-five of these having returned to their families. Of the remainder, four were schizophrenics, two of which did not improve with treatment and were transferred to Cleveland State Hospital, and one child was a mentally deficient psychotic who was committed to the state institution for the feebleminded. We also see that in the group of pure psychoses, twelve returned to their families, eight having received specific therapy, and four having had spontaneous remissions.

Summary

Forty-three youngsters between nine and seventeen years of age, admitted to a receiving hospital, were studied and classified into four groups: psychotic, neurotic, primary behavior disorder, and mental deficiency with psychosis. In a review of the literature, it was seen that the period of adolescence brings on an increase in stress, contributing to outbreaks of abnormal behavior. Schizophrenia was the most frequent

diagnosis of psychosis in children, but any psychotic break before puberty was rarely found. In the group studied, it was seen that there was no consistent difference found in the type of behavior which brought them to the hospital. A discrepancy in the sex ratio in the child group as compared to the adult group in the hospital was noted. Over half of the admissions in the group were for relatively pure psychoses, with schizophrenia predominating. Twenty per cent of the cases were primary behavior disorders who had made over half of the fifty-nine social agency contacts recorded. Broken homes was the most prominent social factor found in these cases with psychosis in the family being the second most prevalent factor in the backgrounds of psychotic children. Twenty-five of the patients have been discharged to their families, while five have been transferred to other state institutions for prolonged care. Twenty-one of the entire group received specific therapy, that is, electric shock therapy, insulin coma therapy, or intensive psychotherapy, with improvement in fifteen of these cases. It is encouraging to note the relatively high proportion of discharges in view of the generally poor prognosis of severe mental disorders in the early age groups. However, it must be remembered that many of these youngsters may be expected to have subsequent exacerbations of their illness, with poorer prognosis.

BIBLIOGRAPHY

1. Bleuler, E.: Textbook of Psychiatry (Tr. A. A. Brill), *Macmillan Company,* New York, 1924.
2. Mead, M., quoted in Klineberg, O.: Social Psychology, *Henry Holt and Company,* New York, 1940, page 492.
3. Henderson, D. K., and Gillespie, R. D.: A Textbook of Psychiatry. *Oxford University Press,* New York, 1940, 586-587.
4. Bradley, C.: "Psychoses in Children" in Modern Trends in Child Psychiatry, Lewis, N.D.C., and Pacella, B. L. *International Universities Press, New York,* 1945, 135-154.
5. *Ibid.,* page 136.
6. Bradley, C., and Bower, M.: Behavior Characteristics of Schizophrenic Children. *Psychiatric Quarterly,* 1941, 15, 2, 296-315.
7. Friedlander, K.: The Psychoanalytic Approach to Juvenile Delinquency. *International Universities Press,* New York, 1947.
8. Despert, J. L.: Thinking and Motility Disorder in a Schizophrenic Child. *Psychiatric Quarterly,* 1941, 15, 3, 522-536.
9. Van Ophuijsen, J. H. W.: "Primary Conduct Disturbances" in Lewis, N. D. C., and Pacella, B. L., *op. cit.,* 35-42.
10. Aichorn, A.: Wayward Youth. *Viking Press,* New York, 1947.
11. Childers, A. T.: A Study of Some Schizoid Children." *Mental Hygiene,* 1931, XV, 106-134.
12. Schulz, Bruno: Incidence of Psychoses Among Children Both of Whose Parents had Affective Psychoses." *Ztschr. f. d. Ges. Neurol. u. Psychiat.,* 169:311 (April) 1940, abstracted in *Archives of Neurology and Psychiatry,* 1940, 44, 1327.

Postgraduate Course In Clinical Neurology

Department of Postgraduate Medicine
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN
May 14-17, 1951

The course is designed to re-orient the practicing physician in regard to the nervous system and the disease process affecting it, stressing principally the close relationship between systemic disease in general and nervous system involvement or complications. The procedure of the neurologic examination will be reviewed with special emphasis on some of the newer diagnostic procedures. Many of the nervous system manifestations more commonly met with in general practice will be discussed individually. Diagnostic procedures, differential diagnosis and the newer modes of therapeutic approach will be dealt with. The course will be augmented by clinical presentations and a review of the essential laboratory procedures.

Detailed program may be obtained from

HOWARD H. CUMMINGS, M.D., *Chairman*
Department of Postgraduate Medicine
UNIVERSITY HOSPITAL ANN ARBOR, MICHIGAN